Essays on Innovation, Competition and Regulation in the Pharmaceutical Industry

by

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David Ridley

Dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the Department of Economics
in the Graduate School of Duke University
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Abstract

My dissertation explores the interactions between the various agents in the pharmaceutical industry and how they are affected by changes in health care policy. In my work, I examine innovation and competition among new brand drugs and the value of prescription drug insurance after patent expiration.

The second chapter of my dissertation empirically assesses the trade-off between patent breadth and patent length, a topic that has attracted significant theoretical but little empirical attention. I estimate a model of pharmaceutical demand and supply that incorporates insurance and advertising for the antidepressant market. Using these estimates, I consider the potential welfare effects of giving some of the most important product innovations broader but shorter patents, which increases the market power that these innovators have in the short-run but also allows for more rapid entry by generics. My results indicate that in this setting broader patents could increase total welfare by more than 9%, mostly through savings in insurer expenditures. These results are robust to endogenizing the entry of other branded drugs.

In the third chapter, which stems from research done jointly with Peter Arcidiacono, Paul Ellickson, and David Ridley, I use data from the pharmaceutical industry to estimate demand and supply for prescription drugs across both insured and uninsured consumers, allowing for consumer preferences organized into discrete types. I account for an important characteristic of health care markets: the price

paid by insured consumers (copayment) is typically much smaller than the price received by the manufacturer. This analysis highlights how generic-drug availability differentially affects insured and uninsured consumers. In particular, generic entry disproportionately benefits insured consumers, at least in the first year to two years.

The fourth chapter in my dissertation extends the analysis in Chapter 2 to allow for a more generalized framework. In Chapter 2, the first pharmaceutical product innovation that enters a therapeutic class is assumed to be high-value while those innovations that follow are assumed to provide relatively little, if any, added therapeutic value beyond the first. Using the same data and demand model estimates, I consider the potential welfare effects of allowing these later to be considered high-value products and providing them with greater patent breadth and shorter patent length. My results indicate that in this setting, the modified patent policy could still increase total welfare by more than 8%, mostly through savings in insurer expenditures. These results are also robust to endogenizing the entry of other branded products.

This dissertation is dedicated to my family.

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Symbols

Throughout my dissertation, I use Greek and Roman letters to represent variables in my theoretical and empirical models. These variables often contain subscripts in order to index specific observations. For example, X_{jt} may represent the X value for product j in time period t. With each new variable introduced in the body of my dissertation, I explain what it to refers to and how to interpret any subscripts used.

Abbreviations

Below I list the set of abbreviations used in my dissertation as well as a brief corresponding description for each item.

ADHD	Attention deficit hyperactivity disorder, a psychiatric disorder of not being able to focus, being overactive, not being able control behavior, or a combination of these.
ACA	Affordable Care Act, a U.S. law that among other things, requires an expansion of healthcare insurance coverage to those U.S. citizens that were previously uninsured.
ATC	Anatomical Therapeutic Chemical, a classification system established by the World Health Organization to provide a clear, internationally recognized system by which innovating pharmaceutical firms can determine to which drug class their innovation corresponds.
CAP	Capsule, a common drug formulation.

CCAE	Commercial Claims and Encounters, a database which consists of a nation-wide sample of healthcare insurance claims provided by large employers and health plans.
CDC	The Centers for Disease Control and Prevention, a U.S. agency charged with protecting public health and safety through the control and prevention of disease, injury, and disability.
FDA	Food and Drug Administration, a U.S. agency charged with ensuring a minimum standard of quality of food and drugs that enter U.S. markets.
FOC	First order condition, a condition the helps determine the optimal behavior of an agent in the market.
FOIA	Freedom of Information Act, a U.S. law that allows citizens to obtain non-confidential information gathered by the U.S. government.
GERD	Gastroesophageal reflux disease, a chronic digestive disease that occurs when stomach acid or, occasionally, bile flows back (refluxes) into your food pipe (esophagus).
H2s	H2 antagonists, the first therapeutic class of drugs that treat uclers as well as reflux ("heartburn").
MAOIs	Monoamine oxidasse inhibitors, the first therapeutic class of antidepressant drugs.
NDC	National Drug Code Directory, a database maintained by the U.S. Food and Drug Administration on producers, repackagers, and distributors of pharmaceutical products.
NGAs	New Generation Antidepressants, the fourth therapeutic class of antidepressant drugs.
OTC	Over-the-counter, a segment of the drug market where products are sold directly to a consumer without a prescription from a healthcare professional.
PPIs	Proton pump inhibitors, the second therapeutic class of drugs that treat uclers as well as reflux ("heartburn").
R&D	Research and development, the process by which innovators create new products that can then enter the market.

SSRIs	Selective serotonin reuptake inhibitors, the third therapeutic class of antidepressant drugs.
TAB	Tablet, a common drug formulation.
TCAs	Tetracyclics, the second therapeutic class of antidepressant drugs.
TRIPS	Trade-Related Intellectual Property Rights, an agreement among the members of the World Trade Organization for a common set of international rules on intellectual property rights.

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I am solely responsible for any errors found here.

1

Introduction

My dissertation explores the interactions between the various agents in the pharmaceutical industry and how they are affected by changes in health care policy. The complexity of the pharmaceutical markets, in part, stems from the many agents involved: brand innovators, generic imitators, pharmacies, insurers, doctors, and patients. The interactions between these agents are often complex and imperfectly observed by the rest of the market. Understanding these interactions is made all the more important by the fact that U.S. pharmaceutical expenditures were the fastest growing component of the total national health expenditure in the last two decades and reached a 10% share in 2010 ($260 billion). Moreover, health care expenditures have received a great deal of public attention recently, specifically with the goal of reducing costs. In my work, I examine innovation and competition among new brand drugs and the value of prescription drug insurance after patent expiration.

In the second chapter, I use data from the pharmaceutical industry to provide the first empirical assessment of the trade-off between patent breadth and patent length. These are the standard levers of patent policies, where patent breadth is a measure of the scope of protection and patent length specifies the duration that this

protection can be enforced. While the theoretical literature provides some guidance on what combination of these levers might be optimal, there has been relatively little work using data to measure the possible gains to alternative breadth-length designs.

To implement my analysis, I use a structural model of demand and supply, which allows me to identify how changing patent breadth and length would impact social welfare. Additionally, my analysis accounts for the effect that health insurance has on consumers' prescription drug prices. As insured consumers pay only a fraction of the full retail price for their pharmaceutical products and insurers subsidize the rest, it is important to account for how this would affect their price sensitivities.

Focusing on the market for antidepressants, I consider two policy experiments. For the first, I assume that the first product to enter a therapeutic class is a ground breaking, high-value product, while later entrants into the class provide relatively little, if any, added therapeutic value beyond the first. I then modify the patent of this first product to address the debate in the pharmaceutical policy literature about the value of limiting the development of later entrants. Specifically, I expand the patent breadth and limit the patent length of the groundbreaking antidepressant, Prozac, in order to temporarily delay the entry of the subsequent products in the same therapeutic class into the market. I find that the total social impact of this modified policy is a gain of more than 9%, mostly through savings in insurer expenditures.

The second counterfactual extends the first, by allowing the innovators of the later products to anticipate the impact of the modified policy and reoptimize their entry decisions during their respective drug development processes. Those innovators that abandoned their drugs save their remaining investment expenditures. I find that while some later innovators would still proceed with their drug developments, others are likely to abandon their innovations, depending on their specific development costs. However, the net social welfare effect is still large and positive. Overall, this research indicates the potential for meaningful social gains from exploring these types

of modified patent policies for industries with a slow and costly innovation process.

The third chapter stems from research done jointly with Peter Arcidiacono, Paul Ellickson, and David Ridley, and focuses on exploring how generic-drug availability differentially affects insured and uninsured consumers. Simple logic suggests that generic drugs particularly benefit uninsured consumers. However, I show that this logic might be wrong, because generic prices fall slowly for uninsured consumers, while insurance copayments fall immediately upon generic entry. Being labeled a generic and having a price below the branded drug are sufficient for the insurance copayment to fall, while it is only through competition that the generic price falls. Hence, at least initially, generic entry disproportionately benefits insured consumers.

For our analysis, I estimate demand and supply for prescription drugs across both insured and uninsured consumers, allowing for consumer preferences organized into discrete types. We account for an important characteristic of health care markets: the price paid by insured consumers (copayment) is typically much smaller than the price received by the manufacturer. Our analysis highlights how generic-drug availability differentially affects insured and uninsured consumers. In particular, generic entry disproportionately benefits insured consumers, at least in the first year to two years.

While this chapter does not explicitly consider policy, estimates from our models of demand and supply allow for the examination of policy experiments. Among the potential experiments is examining the welfare impact of the insurance expansion under the Affordable Care Act (ACA or "Obamacare"), as it impacts consumers, producers, and insurers. Insurance expansion creates possible spillovers for manufacturers. In turn, this creates greater incentives for drug producers to enter the market.

The fourth chapter in my dissertation provides an extension of Chapter 2. Specifically, I relax the assumption that later entrants into a therapeutic class provide rela-

tively little, if any, added therapeutic value beyond the first. A notable need for this extension is Lipitor, which was the sixth innovation to enter the therapeutic class of statins (cholesterol drugs), but is the best-selling drug of all time. The highly successful drug Zoloft provides another example as the second antidepressant to target the serotonin reuptake mechanism in the body. In this chapter, I ask the following question: Do the results from Chapter 2 still hold when an innovation that is not first-in-class is considered to be high-value and provided with the modified patent?

In order to implement my analysis, I use estimates from the static model of demand presented in Chapter 2. The model allows for the quality of products to be determined by consumer preferences. It is then assumed in the policy experiments which products are high-value innovations and which are not. I consider two policy experiments, which correspond to the two experiments in Chapter 2. The experiments expand the patent breadth and limits the patent length of multiple high-value innovations. Effectively, this works by simply tranferring the expanded breadth from an earlier high-value product to a later one that proved to provide significant added therapeutic value. I find that while the net social welfare gains in both policy experiments are lower than those presented in Chapter 2, they are still positive and large. Therefore, these results indicate the potential for meaningful social gains from exploring modified patent policies in a more realistic setting.

2

Patent Breadth Versus Length: An Examination of the Pharmaceutical Industry

2.1 Introduction

Innovation is a primary source of growth for social welfare. Often, innovation is spurred by patents, which confer market exclusivity to innovators. The aim of patent policy is to maximize social welfare by balancing the two competing forces that correspond to this exclusivity: the increasing incentive to innovators and the increasing social cost from market distortions. The standard levers of these policies are patent breadth (the scope of protection), which restricts competitive imitation, and patent length, which specifies the amount of time the protection can be enforced. While the theoretical literature provides some guidance on what combination of these levers might be optimal, there has been relatively little work using data to measure the possible gains to alternative breadth-length designs. In this chapter, I use data from the pharmaceutical industry to provide the first empirical assessment of the trade-off between patent breadth and patent length.

The U.S. pharmaceutical industry is a particularly relevant setting in which to

examine modifications to patent policy. Pharmaceutical companies rely heavily on patents to safeguard innovator profits and there has been an on-going debate over the possible need for innovation-related policy reform.[1] The debate revolves around the idea that there are two types of pharmaceutical product innovations: those that involve groundbreaking new therapies and major improvements over existing products and much more incremental innovations that provide little, if any, added therapeutic benefit.[2] Despite this difference, both types of innovations require substantial investment to develop (DiMasi et al., 2003). Critics of the current policy argue that this latter group of innovations, often referred to as "me-too" products, provide insufficient social benefits to warrant these substantial costs and contribute to the rising costs of health care.[3] My work directly informs this debate by asking the following question: What is the impact on the market of giving some of the most important product innovations broader but shorter patents, which limit the profitability of "me-too" products but allow for more rapid entry of generics?

To estimate the welfare implications of modifying patent breadth and length, I employ a structural approach. While historically there have been a number of patent policy modifications significant to the pharmaceutical industry, none of these occurred in recent decades. Taking a structural approach allows me to identify how changing patent breadth and length would impact social welfare. Existing theoretical work points out that product substitutability and market competitiveness affect the optimal balance of patent breadth and patent length. I begin by estimating a model of demand and supply with differentiated products. My framework accounts for the effect that health insurance has on consumers' prescription drug prices. For

[1] This debate is primarily targetted to innovation of small-molecule drugs, as opposed to biologics, which differ in how innovation and patenting are conducted. For this reason, this chapter focuses exclusively on small-molecule drug markets.

[2] This distinction is also recognized by other countries, including Canada (Lexchin, 2006).

[3] See Kessler et al. (1994), Relman and Angell (2002), Hollis (2004), Angell (2005), Goozner (2005), and Gagne and Choudhry (2011).

pharmaceutical products, insured patients pay only a fraction (the copay) of the full retail price. Therefore, ignoring this feature runs the risk of underestimating consumers' price sensitivities and distorting the results of any subsequent analyses that build on these estimates. Using the model estimates, I then examine the implication of the modified policies on welfare through counterfactual simulations.

For a patent policy to be feasible, the measure of patent breadth must be defined in such a way that it is known to the market and independent of any decisions made by the firms. Hence, in a practical setting, there are only a limited number of available levels that can be used for breadth. I consider a specific set of modifications that are available for the pharmaceutical market. Given that patent breadth in the pharmaceutical industry is already specified in the narrowest feasible terms, the basic counterfactual expands the breadth of a groundbreaking (high-value) drug's market exclusivity by temporarily blocking from the market subsequent drugs that provide little, if any, added value ("me-too"s). This expansion, which leads to increased profits for the high-value innovator, is balanced by a reduction in patent life in order to make her indifferent between the two policy settings. Once the patent for the high-value drug has expired, the "me-too" drugs as well as the generic versions of the high value drug are allowed to enter the market. Effectively, this counterfactual delays market entry of "me-too" drug innovations and advances generic entry on the high-value drug. In this way, I propose to shift incentives, and consequently R&D investment, away from "me-too" innovations to those that are greater in value. I then examine the net impact on drug producers (innovators and manufacturers), consumers, insurers, and overall social welfare.

My analysis focuses on the market for antidepressants. Antidepressants constitute one of the best selling pharmaceutical markets of the past two decades and are exclusively comprised of prescription drugs. I use data containing monthly U.S. pharmaceutical prices and quantities for retail prescription sales as well as national

advertising expenditures, for the period 1991 to 2010. These data capture the evolution of the dominant therapeutic drug class, from the pioneer molecule to the entry of subsequent molecules and the eventual generic entry on nearly all of the top selling molecules.

I estimate own-price elasticities, based on consumer copays, in the range between -1.6 and -3.2. As expected, I find much higher cross-price elasticities among drugs that are similar in the way they function versus those that are not. This suggests that if the modified policy is targeted to a specific grouping, it will have limited impact on products outside of that grouping.

Using estimates from the static models of demand and supply, I consider two policy experiments. The first modifies the patent of the first-in-class groundbreaking drug to address the debate in the pharmaceutical policy literature about the value of limiting the development of "me-too" drugs.[4] Specifically, I expand the patent breadth and limit the patent length of the groundbreaking antidepressant, Prozac, in order to temporarily restrict the subsequent "me-too" products in the same therapeutic class from entering the market. I find that the patent life of Prozac is shortened by nearly six years (70 months). Additionally, the $3.8 billion in lost profits (64%) suffered by "me-too" innovators is overshadowed by the $10.2 billion in savings (14.4%) realized by insurers. Finally, consumers experience a welfare gain of $312 million (1.6%) under the modified framework. The total social impact of this modified policy is a gain of more than $10.6 billion (9.4%).

The second counterfactual extends the first, by allowing the "me-too" innovators to anticipate the impact of the modified policy and reoptimize their entry decisions during their respective drug development processes. Those innovators that abandoned their drugs save their remaining investment expenditures. I find that while

[4] In this chapter, I assume that all products that enter after the first-in-class are "me-too"s. At the end of the chapter, I discuss on-going work in which this assumption is relaxed and these subsequent entrants can be recognized as high value products.

Zoloft would always proceed through Phase III clinical trials and onto the market, Paxil and Celexa would do so with probabilities of only 48.5% and 88%, respectively. The net effect on producers is a slight gain ($178 million or 1.1%) due to the expenditures saved by entry re-optimization. In cases where the products do not enter the market, consumers lose the value of their entry as well as the generics that would have followed on each molecule. However, this loss is still overshadowed by the gain of earlier generic entry on Prozac's molecule, fluoxetine ($194 million or 1%). Insurers realize even greater gains ($10.9 billion or 15.4%) as consumers who would have otherwise purchased Paxil and Celexa, turn to generic fluoxetine instead. The net social welfare effect sums to $11.4 billion (10.1%). These results indicate the potential for meaningful social gains from exploring modified patent policies.

While this is the first empirical study of the tradeoff between patent breadth and length, some aspects of the problem are not addressed. For example, this chapter does not try to address the question of whether initial innovators should be rewarded more generous patents; instead, like most of the theory literature, it considers how to give the initial innovator a fixed reward. Additionally, the analysis includes only a limited range of dynamics. While "me-too" innovators are allowed to reoptimize their entry decisions, the decisions of other market participants are assumed to be exogenous and held fixed. Finally, all follow-on products that enter prior to Prozac's patent expiration are assumed to be "me-too"s. At the end of the chapter, I discuss ongoing work that seeks to address this last limitation.

I proceed in the chapter by first presenting the related literature, which is comprised of the theoretical work on optimal patent design as well as the empirical work aimed at quantifying the effects of competition and social welfare in the pharmaceutical industry. In Section III, I then describe the salient features of the pharmaceutical industry, the data sets, and the market for antidepressants. I present the static models of demand and supply in Section IV and the estimation procedure in Section V.

In Section VI, I describe the results and their implications for the counterfactual simulations. Finally, I implement the counterfactual simulations to measure the welfare implications on consumers, insurers, and producers (innovators and manufacturers) in Section VII.

2.2 Related Literature

This section reviews the relevant literature and contrasts it with the policy simulations in this chapter. The theoretical literature has provided important insights on the underlying determinants of optimal patent policy, particularly with regard to the combination of patent breadth and patent length. Despite the theoretical foundation, relatively little applied work has considered this trade-off.

2.2.1 Theory of Optimal Patent Design

Substantial theoretical work has been done to examine incentives to innovation and the social value of patents.[5] The segment of the literature relevant to my work analyzed how the balance between patent breadth and patent length influences social cost for a given stand-alone product innovation.[6] These papers employed stylized models to highlight the importance of the market structure and the shape of the demand curve in determining optimal patent policy. The market structure is broadly defined to include whether products are differentiated, the number of potential innovators, and the nature of innovation and production costs.[7] For a given innovation,

[5] For a comprehensive review of this literature, see Rockett (2010).

[6] Stand-alone innovation refers to the final market product being composed of one innovation. Other segments of the literature have considered products that are comprised of a combination of different innovations (Scotchmer, 1991; Green and Scotchmer, 1995; O'Donoghue et al., 1998; Bessen and Maskin, 2009) and optimal patent policy with different combinations of policy levers, including patent length alone (Nordhaus, 1969; Scherer, 1972; Nordhaus, 1972), patent length with compulary licensing (Tandon, 1982), patent renewals (Cornelli and Schankerman, 1999), and menues of patents (Cornelli and Schankerman, 1999; Hopenhayn and Mitchell, 2001).

[7] The literature has considered various settings, including: one innovator and many potential imitators in homogeneous products markets (Gilbert and Shapiro, 1990; Gallini, 1992); multiple

the shape of the demand curve reflects consumers' product substitution behavior. The greater this substitutability, the more sensitive consumers will be to a product's price increases and thus, the lower the price that will maximize the innovator's profit. In this way, the shape of the demand curve defines how much profit the patentholder can extract under a given policy.

Many of the relevant papers in this literature share two common features in their approach to optimal patent policy. First, they examined the optimal combination of patent breadth and length that guarantees an innovator a given reward, rather than determine what that award should be.[8] Thus, in a given market, the optimality of a patent policy lies in its ability to minimize social costs while providing sufficient incentive to the innovator. The second key feature is the assumption that demand is independent of patent policy. This means that consumers are expected to purchase and consume products as needed and do not substitute across time.[9]

I focus on a differentiated product market with multiple potential innovators and imitators, along with insurers and two types of social costs, deadweight loss and entry cost (cost of innovation or imitation). Using a differentiated product market with heterogeneous consumers, Klemperer (1990) showed that if consumers all have the same transportation costs, social cost primarily stems from deadweight loss, making narrow patents with long lengths optimal. Alternatively, if consumers all have the same valuation of products, then social cost primarily stems from substitution to less preferred products, and broad patents with short lengths are optimal. Drawing

innovators that develop differentiated products (Klemperer, 1990; Wright, 1999); and costly innovation or imitation (Gallini, 1992; Wright, 1999).

[8] This implies that the total profit earned by the innovator under patent protection is necessary to induce the given level of innovation. The patentholder's net present discounted profit V earned under patent protection is therefore set to be nondecreasing. The significance of this restriction, which amounts to a form of Ramsey pricing, lies in its implicit assumption that the long-run innovation flow is not reduced regardless of the policy chosen (Ayres and Klemperer, 1999).

[9] If consumers could substitute across time, the roles of patent breadth and length would be more similar (Klemperer, 1990).

on these insights, I start by estimating the demand parameters to determine the substitutability of products to others on the market as well as to the outside good.

The impact of high entry cost was also considered by the literature. Gallini (1992) considered a market in which imitators pay an entry cost and produce perfect substitutes that don't infringe on the innovator's patent. If patent breadth increases imitators' entry cost, then the optimal patent policy was shown to consist of broad patents with short lengths. Allowing these entry costs to differ among the imitators, Wright (1999) found that the optimal patents could have narrow breadths and long lengths if deadweight loss is monotonically decreasing in the number of imitators. Otherwise, if deadweight loss were nondecreasing in the number of imitators, broad patents with short lengths would be optimal. To account for the presence of high entry cost and its potential effect on the modified patent policy, I compare innovators' discounted profits to their innovation costs. Cases in which the cost exceeds the profit indicate that the innovators would be better off not entering the market.

2.2.2 Empirical Literature

The empirical literature relevant to the search for optimal patent policy includes reduced form and structural papers aimed at quantifying the effects of competition and social welfare in the pharmaceutical industry.[10] The first strand of this literature examined natural experiments stemming from changes to patent policy in the U.S. and other countries in order to better understand the potential welfare implications of policy changes. The most notable of the U.S. policy changes is the adoption of the Hatch-Waxman Act (1984). In streamlining the process and reducing the costs of generic entry, this law not only ensured that firms with profitable products would face generic competition after patent expiration, but also reduced the average

[10] In this subsection, I provide a brief overview of the relevant empirical literature. For a more comprehensive review, see Cohen (2010) and Hall and Harhoff (2012).

time for generic entry after patent expiration from three years to only three weeks (or less) (CBO, 1998; Schacht and Thomas, 2005; Grabowski and Kyle, 2007). In some cases, challenges under Paragraph IV of the Hatch-Waxman Act allow generic firms to enter the market prior to the patent expiration date originally claimed by the innovator. Branstetter et al. (2011) estimated that paragraph IV challenges led to a substantial net social gain in the hypertension market over the last decade. Grabowski and Kyle (2007) examined the decrease in the average amount of time brand name pharmaceuticals enjoy on the market before generic competition and found that this shift is even more pronounced in larger markets with blockbuster drugs.[11] Focusing on the international stage, Sakakibara and Branstetter (2001) examined the impact of the 1988 patent reforms in Japan on the country's innovative effort. The authors found little evidence that the uniform expansion of patent scope led to greater R&D effort by domestic innovators.

The other strand of relevant literature utilized structural frameworks to implement counterfactual simulations.[12] A few papers have estimated the value consumers place on having follow-on products and/or generics in the market. Using data for the ADHD drug market, Bokhari and Fournier (2012) found that generic entry led to a significantly larger welfare increase than entry by follow-on products. Arcidiacono et al. (2013) found that "me-too" anti-ulcer drugs increase insurer spending by billions of dollars each year. Next, Chaudhuri et al. (2006) and Dutta (2011) applied a structural framework to estimate the effect that the Trade-Related Intellectual Prop-

[11] One concern discussed in the literature is that this type of reduction in market exclusivity for patented products has decreased the incentives for future innovators. For more details, see Grabowski and Kyle (2007), Higgins and Graham (2009), and Panattoni (2011).

[12] These papers examined demand through a variety of discrete choice models, including nested-logit (Stern, 1996b; Mortimer, 1998; Azoulay, 2002; Currie and Park, 2002; Dutta, 2011), principles of differentiation generalized extreme value (Arcidiacono et al., 2013), random coefficients (mixed) logit (Cleanthous, 2002; Dickstein, 2011; Yin, 2013) and the almost ideal demand system (Ellison et al., 1997; Chaudhuri et al., 2006; Bokhari and Fournier, 2012). Several papers also incorpoate physician/patient learning into their frameworks (Ching, 2010b,c; Dickstein, 2011).

erty Rights (TRIPS) would have on pharmaceutical industry in India. These papers found that the new patent rules will lead to substantial loss to consumer welfare and a relatively small gain to foreign patent holders. However, these results reflect short-term estimates, couched in the presumption that domestic firms will not engage in any significant innovative activity. Incorporating consumer learning into the analysis, Ching (2010c) found that shortening the time between patent expiration and generic entry leads to a very small welfare gain for consumers. Finally, the closest work to this chapter was provided by Yin (2013), who estimated the welfare effects of granting additional periods of exclusivity to original innovators who make incremental improvements to their own existing products (e.g. new drug formulations, new indications, or improved efficacy and safety).[13] Using the market for antidepressants, Yin (2013) found that while the value of the incremental innovations in aggregate is greater than the corresponding costs, some products netted a social loss.

This chapter differs from and contributes to the empirical literature in two ways. First, I look specifically at the tradeoff between patent breadth and length that has been the focus of the theoretical literature. In this way, I attempt to limit the impact of any patent modification on long-run innovation flow. Second, I explicitly consider different ways of handling how a modified policy would impact the entry of later drugs.

2.3 Background and Data

In this section, I provide background information relevant to the market structure and briefly detail the multiple datasets that allow me to implement the counterfactual simulations. First, I describe the key features of the U.S. Pharmaceutical industry and explain why it is particularly suitable for an examination of a modified patent

[13] The estimation framework used by Yin (2013) is very similar to the one proposed by Dunn (2012), which found that the quality-adjusted price in the anti-cholesterol drug market decreases with the introduction of new product innovations.

policy. I then present information on the antidepressant market, which serves as a good application for my analysis, given that the data captures the evolution of the dominant therapeutic drug class.

2.3.1 The U.S. Pharmaceutical Industry

The U.S. pharmaceutical industry differs from most other industries in several important ways. First, new products in this industry are expensive to develop and cheap to produce, which implies that the industry is highly dependent on patents to safeguard innovators' profits and that it may be more socially efficient to limit development of all but the most valued innovations. As part of the development process, innovators must prove that their products are sufficiently safe and effective in order to enter the market. However, innovators (pioneers and followers) only need to compare the efficacy of their products to either long-established quality minimums or placebo control groups. Thus, products following the pioneer can enter the market with equivalent, or even inferior, quality. As depicted in Figure 2.1, the drug development process can take more than a decade, and require thousands of patients, to complete. DiMasi et al. (2003) estimated that the average out-of-pocket cost of this process for successfully developed and approved products amounted to several hundreds of millions of dollars, after accounting for risk of failure. On the other hand, marginal manufacturing costs per dose tend to be less than one or two dollars, if not just a few cents. Moreover, given that product development predominantly occurs after the innovation has been patented, a product generally has between eight and 14 years of patent protection remaining once it reaches the market (this period is commonly referred to as the effective patent life).

Second, each pharmaceutical product innovation is generally distinct in molecular structure from other product innovations, even though they may be used for the

exact same purpose and be very similar in quality.[14] Under the current policy, each pharmaceutical patent protects the active component of the molecule and allows the innovator to generalize on the weak or inert components that may be combined to it. While technically a patent can be further narrowed in scope to all complete molecules, this would amount to a substantial burden on innovators, since the innovation tends to be fully embodied in the active component and the rest represents little more than filler. In this way, pharmaceutical patents represent as narrow a scope for patent protection as is feasible (henceforth, I refer to this measure of patent breadth as the molecule level).

The next key feature of this industry is that pharmaceutical product innovations are patented before their value is known, normally at the beginning of the development process (Mossinghoff, 1999; Grabowski, 2002). Usually, by the end of Phase II, innovators have gained their first significant evidence of efficacy and safety (DiMasi et al., 1991; Mossinghoff, 1999). This means that innovators might wait as long as seven or eight years after applying for the patent before they know the value of their product, and another four to five years before they can enter the market (see Figure 2.1). The temporal disconnect between these events means that a "me-too" innovation will be patented before it is known to be a "me-too". For this reason, the conventional framework of patent policy needs to be adapted to focus on which products may enter the market, rather than strictly specifying the products that are owned by a given innovator. The need to exclude the ownership requirement stems from the molecular differences between the groundbreaking and "me-too" innovations, which are described above. In practice, greater patent breadth on high-value innovations would mean that innovators of "me-too" products would still retain their patents, but be restricted from entering the market.

[14] Exceptions to this include the type of incremental improvements innovators make to their own products in order to get additional periods of exclusivity. This paper focuses on small molecule (non-biologic) patents that identify the chemical structure and activity of a new compound.

A fourth key feature is that products belong to therapeutic classes, which are categorized according to the mechanism or chemistry that the products target in the body and, typically, more than one therapeutic class is used for a specified treatment. In this way, there is a limit to the degree to which two products in the same therapeutic class can be differentiated. Given that this classification is independent of any decisions made by the firms, it provides a clear level to which breadth could be expanded from the current molecule level. The only other potentially feasible level that breadth could take in this context would be to encompass the full antidepressant market, but still allow prior market entrants to remain.[15]

Next, entry in this industry by generic drug competitors once the patent has expired provides substantial cost savings to consumers. Indeed, generic entry has been observed to reduce a molecule's average price by as much as 80% within 18 months after expiration (Jena et al., 2009). Competitive pressure stems not only from the number of generic entrants, but also from state laws that permit or require pharmacists to dispense an available generic version, unless expressly prohibited by the perscribing physician. Therefore, as long as developers of high-value drugs have sufficient incentive to innovate, enabling earlier generic entry on these drugs to occur will allow consumers to enjoy these gains that much sooner.

The final key feature of the pharmaceutical industry is that most consumers generally pay only a small fraction of a product's full price, called the copayment or copay, while their prescription insurer pays the rest. For this benefit, consumers (or their employers) regularly pay a premium to their insurer. With the market power that results from covering many consumers, insurers are then able to negotiate

[15] While I ignore the possibility that a drug may be used for multiple completely different markets (treatments), it is a simple matter to focus the entry restriction to only a specified market and still allow access in other markets. For example, the popular hair treatment Rogaine (minoxidil) is also used to treat high blood pressure (under the trade name Loniten). Even if it had temporarily been blocked as a high blood pressure medication, as the first hair growth drug approved by the FDA, it would be free to enter this second market.

reduced prices with the drug manufacturers, often in the form of a rebate. I discuss the available data below.

2.3.2 Data

To analyze this market, I combine several data sets. I acquired the first from SDI Health (hereafter, "SDI").[16] This data contains monthly, national-level revenue and quantities for prescription drug sales by retail vendors, over the period 1991 to 2010. Observations are broken down by individual drug, identified by either its brand name or as a generic, its formulation (i.e. capsule, tablet, etc.), the dose size, and the manufacturer that produced it. While this data takes into account discounts, it does not include rebates.[17] For this reason, retail prices may not represent the effective product prices, but they are the best data available to the public.[18] Additionally, the SDI data does not include sales through hospitals or prescriptions provided to consumers directly from third party institutions, such as psychiatric institutions and the military.[19]

A drawback of the SDI data is that it reflects information reported by retailers, rather than by manufacturers. Hence, the data does not consistently capture changes in ownership among manufacturers and also includes sales attributed to firms that

[16] Shortly after this data was purchased, SDI Health was acquired by IMS Health.

[17] As previously discussed, rebates are direct payments from drug manufacturers to health care providers and they represent another dimension in which patented molecules can compete for sales. Unlike discounts, which are observed by the entire market, rebates are generally kept confidential between the two entities in the agreement.

[18] While rebate data are not publicly available, some inference can be made on their bounds and volatility. Under the Medicaid Drug Rebate Program, branded drug manufacturers must give the U.S. government either 15.1% off of their average price or their best rebated price, if it is lower. Hence, it is likely that manufacturers only rarely exceeded this threshold prior to generic entry on the drug (Arcidiacono et al., 2013). Additionally, it is likely that rebate agreements between manufacturers and insurers are generally negotiated on an annual or semiannual basis, which limits their impact on volatility in the national average price per drug.

[19] Expenditures through third party payers, including the military, ranged between 3% and 5% of total national expenditures between 1991 and 2010. Additional information can be found through the Centers for Medicare & Medicaid Services website: http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html.

merely package or distribute the pharmaceuticals, rather than the true manufacturers. To remedy the issue with changes in ownership, I conducted an extensive search through public filings and company websites to identify mergers and acquisitions among the relevant firms. To address the second issue, I use the FDA's National Drug Code Directory (NDC) database to determine firm affiliations according to two key identifiers, NDC Number and Application Number. Given the sparsity of the historical data available on the FDA's website, I obtained a more comprehensive dataset through a Freedom of Information Act (FOIA) request.[20]

I acquired the second data set that I use from Encuity, Inc. This data includes monthly, national-level advertising to physicians, nurse practitioners, and physician assistants (also known as "detailing"). It is generally understood that marketing strategies for branded drugs include a great deal of detailing expenditures, while generic manufacturers rarely engage in this practice. It should be noted that generics are not necessarily considered perfect substitutes by consumers for many reasons, including brand loyalty and preferences for formulation, flavor, and even color.[21] However, their efficacy and side effect profiles should be very similar, if not identical, to their branded counterparts, for any given molecule. Due to some data limitations, I do not include advertising that directly target patients. However, the effect if this is likely mitigated by the fact that patients and doctors generally make the product decisions together and I include advertising to physicians.

Finally, I use the MarketScan Commercial Claims and Encounters (CCAE) Database, obtained through the National Bureau of Economic Research, which consists of a nation-wide sample of healthcare insurance claims provided by large employers and

[20] Additional information on the historical data available through the FDA's website can be found at www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm.

[21] Ching (2010c) and Ching (2010b) provide some support that consumers preceive this difference between a brand product and its generic versions. These papers argue that consumers are initially uncertain about the quality of generics and that the rate of generic diffusion is explained by consumers learning from others' use.

health plans. This data set is comprised of patient-level prescription drug purchases between 1996 and 2009. It includes patient copay expenditures per prescription as well as some corresponding insurance plan information. However, the consumer premiums paid to insurers are not available.

2.3.3 The Antidepressant Market

Major depression or lower-level chronic depression affects 9.1% of adults in the United States.[22] However, according to The National Ambulatory Medical Care Survey, the number of people receiving treatment for depression tripled between 1987 and 1997. In studying this trend, Olfson et al. (2002) noted that this substantial increase "coincided with the advent of better-tolerated antidepressants, increased penetration of managed care, and the development of rapid and efficient procedures for diagnosing depression in clinical practice." These concurrent events imply that the new drugs to the market were of higher quality, and consumer costs were reduced by the increase in insurance coverage and the improved diagnostics. Figure 2.2 shows that drug sales in this market increased substantially over time. Antidepressants are generally categorized into four main therapeutic classes. Each class targets a different mechanism in the body in order to elicit the desired effect.

The first two of these classes are generally considered by the medical literature to be first-generation antidepressants. In the early 1950's, monoamine oxidase inhibitors (MAOIs) were found to reduce the symptoms of depression and were introduced as a treatment. However, MAOIs were temporarily taken off the U.S. market when it was discovered that under specific conditions, the drug could cause death. The promise

[22] See the Centers for Disease Control and Prevention (CDC) revised estimates for more details (www.cdc.gov/features/dsdepression). Prevalence rates identified in other papers vary. Dickstein (2011) cites a prevalence of 6.5% for adults affected by major depression, Berndt et al. (1996) note survey evidence that indicates a 9% prevalence rate for major and lower-level chronic depression among the employed labor force, Greenberg et al. (2003) use the Epidemiologic Catchment Area survey to support a 10.1% rate, and Kessler et al. (2005) find a rate of 8.2% across all adults.

of MAOIs led to continued research on treatments for mental illness. By the 1970's, tetracyclics (TCAs) had been shown to increase the brain's supply of norepinephrine and serotonin and were introduced as the second therapeutic class. While not as likely to cause death, TCAs offered little added benefit in efficacy and contributed to a host of other side effects that range from mild to severe.

The second-generation antidepressants include the last two classes. The most prominent antidepressant class consists of selective serotonin reuptake inhibitors (SSRIs), which elevate only serotonin in the brain. While SSRIs did not offer significant benefit in efficacy over MAOIs or TCAs, their side effects were not nearly as frequent or severe. Little more is known about the true way that these chemicals influence depression. The last class is also the least well understood. This class is often referred to as Other Antidepressants or as New Generation Antidepressants (NGAs). NGAs appear to allow for increased levels of norepinephrine and dopamine in the brain. Nearly all of the products sold under patent during the date range of the SDI data belong to either the NGAs or SSRIs.

Figures 2.2 and 4.1 provide monthly totals of daily-dose sales by therapeutic class and molecule, respectively. While the TCAs are the dominant drug class at the start of my time period, they experienced a steady decline thereafter. Conversely, the NGAs drew a sizable share of the market during the same time period with the introduction of several new molecules. However, the SSRIs clearly became the dominant class of antidepressants. MAOI sales are included in Figure 2.2, but are too small to see. Figure 4.1 illustrates how quickly sales for branded molecules can be overtaken by their generic counterparts after patent expiration. Prozac's patent expired in mid-2001 and within a few months, most of fluoxetine sales were made by generics. Similar switching can be observed for Zoloft and Celexa.

The SSRIs began in 1988 with the market introduction of Prozac, which immediately became the dominant product in the market with annual sales of over $1

billion. Figure 2.4 shows weighted average prices for SSRI products, presented at the daily-dose level in 2010 dollars. Following on Prozac's success, Zoloft was released in early 1992 and competed at a price that trended downward, falling below Prozac's price by the end of 1995. Then Paxil, in the beginning of 1993, and Celexa, in the second half of 1998, were each released with prices significantly higher than either Zoloft or Prozac. The remaining SSRIs entered the market after Prozac's patent expiration. It is important to note that generic prices on each of the first four SSRIs (denoted by the dashed lines) begin close to their brand counterparts and then quickly drop thereafter. Specifically, average daily-dose price for generic variations of Prozac (fluoxetine) starts at a high of $3.07 and falls to $0.76 within 18 months.

As previously mentioned, advertising is an important component of competition in the pharmaceutical industry. Firms spent an average of $8.5 million per month to advertise Prozac, Zoloft, and Paxil to physicians during the molecules' patent protected period. However, there were small increases in advertising for Zoloft and Paxil around the time of Prozac's patent expiration. This suggests that firms that correspond to these drugs were attempting to limit consumer switching from their respective products to generic variations of fluoxetine. Advertising expenditure was nearly double the average amount for Lexapro. For each brand name, advertising quickly tapered off after its patent expired. Interestingly, this tapering off of brand advertising provides a countervailing effect that balances with the lower generic pricing. This likely explains why total quantity sales on many molecules remain stable in the years around a brand's patent expiration. Generic manufacturing firms might advertise only if they are the first to enter on a given molecule and then stop once other generics enter the market.

The comparison between the prescription-level retail prices and the copays paid by patients is presented in Table 4.1 for a selected sample of the top sellling NGA and SSRI drugs. The average retail price for a prescription of brand drugs tends to

be over $100, while an insured patient's expense ranges between $15 and $30. This means that insurers pay the vast majority of the cost of these prescription drugs. The retail prices of generics tend to be about half the price of the branded drugs, if not less. For generics, insured patients pay around $10. Also included in the table are the dates that the molecules first launched onto the market and their first patent expiration dates.[23] Next, are the number of generic producers that compete under a given molecule. Note that while generic manufacturers do provide a great deal of price competition, these products may still be differentiated by formulation and manufacturer.

The antidepressant market provides a particularly useful example in examining modified patent policy for a few reasons. First, the market consists almost entirely of prescription drugs, which implies that sales are more likely to be captured in the data. Second, sales in the antidepressant market over the period 1991 to 2010 were dominated by SSRI manufacturers, which mostly consisted of large pharmaceutical firms that relied on patent protection to prohibit generic competition. Finally, the data captures the competitive evolution of the dominant therapeutic drug class. While the entry of the pioneer molecule in the SSRI class is not observed, the data does capture the entry of all subsequent products. I examine the impact of broadening Prozac's patent's breadth while simultaneously shortening its patent length in order to reduce incentives for the some of the subsequent SSRI entrants, which I assume to be "me-too" products. Once these profits are earned, the modified patent would expire and allow both generic competitors and the available "me-too" products to enter.

[23] As previously mentioned, innovators occasionally patent new formulations of their products in an effort to extend their market exclusivity.

2.4 The Model

In this section, I present a static model of differentiated-product demand and supply which will be used to determine the shape of the demand curve and recover the implied marginal costs. Building off of Berry (1994) and Cardell (1997), I estimate demand using a three-level nested-logit model, which adequately provides the flexibility of substitution patterns that will be applied to the counterfactual simulations. I then apply these estimates to a supply model and equilibrium conditions similar to those proposed in Nevo (2000a). This approach allows me to implement the modified policies by simply removing products from the market and then reoptimizing price to equilibrium.

2.4.1 Product Price and Consumer Copay

As presented in the previous section, the copay paid by insured consumers for product j at time t, given by c_{jt}, tends to be substantially lower than the price the set by manufacturers, p_{jt}. Insurers generally assign drugs to three copay tiers, based on their relative prices. High priced brand drugs tend to be assigned to the top tier (non-formulary), which may have a copay around \$50 per prescription, while more moderately priced brands are assigned in the second tier (formulary) may have a copay of \$30 per prescription. The final tier is for generic drugs, which tend to have a copay of \$10 per prescription (see Table 4.1). Since these assignment decisions are likely independent of any specific drug or class of drugs, I treat them as given. Moreover, I assume that insurers play a passive role, limited to their payment expenditures on consumer purchases.

I model the relationship between copay and price as a power function with a power value less than one (Arcidiacono et al., 2013).[24] In particular, I assume the

[24] The power function dampens high prices, which matches the trends observed in the data.

form

$$c_{jt} = p_{jt}^{\phi} \cdot e^{\gamma_0 + X_{jt}^{c}\gamma_1} + \nu_{jt}, \tag{2.1}$$

where X_{jt}^{c} are observed product characteristics, ν_{jt} is an error term, and $\{\phi, \gamma_0, \gamma_1\}$ is the set of parameters to be estimated.

2.4.2 The Demand Side

Suppose consumers choose from an assortment of products which belong to two levels of nests (or groups). Let g index the nests in the upper level and m_g index the groups in the lower level, the subnest. While consumers consider all of the products in their choice set, products within a nest (or subnest) are more similar in value than those across nests (or subnests). Within this three-level nested logit framework, a consumer is assumed to first choose a nest g (a therapeutic class), then a subnest m (a molecule) from those available in g, and finally a product j from those within subnest m.[25]

The indirect utility that consumer i gets from product j at time t is given by

$$u_{ijt} = \delta_{jt} + \psi_{ijt} \tag{2.2}$$

$$\text{where} \quad \delta_{jt} = X_{jt}\beta + \alpha c_{jt} + \gamma ln(a_{m_g t}) + \xi_{jt} \tag{2.3}$$

$$\text{and} \quad \psi_{ijt} = \zeta_{ig} + (1-\sigma_g)\zeta_{im_g} + (1-\sigma_g)(1-\sigma_{m_g})\varepsilon_{ijt}. \tag{2.4}$$

The first term in equation (2.2) is the mean utility level of product j, which is a function of observed product characteristics (X_{jt}) and those characteristics which are observed by consumers but not by the econometrician (ξ_{jt}). The mean utility also includes the consumer's copay, c_{jt}, and the natural log of the advertising, $a_{m_g t}$,

[25] In order to avoid the complexity of decision-making and consumption involved in this setting, I assume that the "consumer" includes both the prescribing doctor and the patient who uses the medication, and that patients are fully compliant in using all of the prescribed medication they purchase. Dickstein (2011) employed a dynamic learning model that relaxes both of these assumptions. Additionally, I assume that a "producer" includes the drug manufacturer as well as the pharmacies that sell its product to consumers. Both of these assumptions are common in the literature.

for product j.[26] Since firms may offer multiple products within the same subnest m, I assume that a firm simultaneously advertises this collection of products and index advertising accordingly.

The other term in equation (2.2) is the heteroskadastic error, which captures the effects of the random taste parameters and reflects the form of the nesting structure. For consumer i, ζ_{ig} and ζ_{im_g} capture the unobserved variation common to all products indexed by g and m, respectively. Within the bounds of [0,1), σ_g and σ_{m_g} measure the importance of the structure that defines each nest (subnest) as being distinct from the rest of the sample. As σ approaches one, the products in the same nest (subnest) can be considered stronger substitutes, than products across nests (subnests). If σ is zero, preferences for the products within the nest (subnest) are not correlated in any way distinct from the rest of the products and the model simplifies to either the nested logit (if σ for only one of the levels is zero) or the standard logit model (if both).

Finally, ε_{ijt} represents the distribution of consumer preferences around the mean valuation ξ_{jt} and is assumed to be an identically and independently distributed (i.i.d) extreme value. Cardell (1997) shows that ζ_1 and ζ_2 have unique distributions, such that if ε is an extreme value random variable, then so is $\zeta_1 + (1-\sigma_1)\zeta_2 + (1-\sigma_1)(1-\sigma_2)\varepsilon$. Berry (1994) and Nevo (2000b) note that an important implication of the i.i.d assumption for ε_{ijt} across customers and choices is that products in the same nest are solely differentiated by the mean utility levels, δ_{jt}. Hence, market shares and elasticities are solely determined by δ_{jt}. However, when some products are more similar than others, this dependence on just δ_{jt} for consumer choices will result in estimated product substitution patterns that do not match the true patterns.

[26] Allowing advertising to enter the utility function in this way captures the persuasive role it has on consumer choices. However, given the possibility that consumers may be uncertain about the quality of new drugs, advertising might also play an important informative role (Ching and Ishihara, 2010, 2012). In Section 2.5.1, I discuss the use of fixed effects to incorporate consumer learning into the estimation.

The advantage of the nested-logit model over the standard logit model is to lessen this restriction on substitution patterns by grouping products known to be more comparable into nests. Despite its reliance on the *a priori* assumption on how the market is segmented into nests, this framework provides sufficient flexibility on the substitution patterns for my needs.[27] Another feature of logit models is the S-shaped nature it imposes on demand. Whether firms price in the convex or concave regions is determined by the parameter estimates and costs.

Following the three-level nested logit analog of Berry (1994) and defining $\eta = [1-(1-\sigma_g)(1-\sigma_{m_g})] \in [0,1)$, the demand equation can be restated as

$$\ln(s_{jt}) - \ln(s_{0t}) = X_{jt}\beta + \alpha c_{jt} + \gamma \ln(a_{m_g t}) + \sigma_g \ln(s_{m_g t}) + \eta \ln(s_{jt/m_g}) + \xi_{jt}. \quad (2.5)$$

The first term on the left-hand side is the log of the market share of product j at time t, while the second term is the log of the share of the outside good in the same period. Finally, at time t, s_{jt/m_g} is product j's share of sales by all products in subnest m and $s_{m_g t}$ is subnest m's share of sales by all products in nest g. The derivation of this form of the demand equation is provided in Appendix A.

2.4.3 The Supply Side

Suppose there are F firms, each of which produces some subset, $\mathcal{J}_{ft}$, of the $j = 1, ..., J_t$ different products available at time $t = 1, \ldots, T$. The profit of firm f at time t is

$$\Pi_{ft} = \sum_{m \in \mathcal{J}_{ft}} \sum_{j \in m} [(p_{jt} - mc_{jt}) M_t s_j(\boldsymbol{p}_t)] - a_{mt} - C_{ft} \quad (2.6)$$

where $s_j(\boldsymbol{p}_t)$ is the market share of product j and is a function of the prices of all products at time t. Note that I hold advertising fixed and do not attempt to solve for new advertising trajectories when performing counterfactuals. The market size

[27] The market I focus on experienced a great deal of product entry during my sample period. Given that the Almost Ideal Demand System (AIDS) approach does not have a good way of dealing with a varying number of products, I chose not to use it (Chaudhuri et al., 2006).

at time t is denoted by M_t, mc_{jt} is the marginal cost of production, and C_{ft} is the fixed cost of production.

In line with the literature, I assume that there's a unique Bertrand-Nash pricing equilibrium, with prices that satisfy these first-order conditions.[28] A key feature of this assumption is that it enables me to measure the impact of alternative policies on social welfare. For firm f at time t, let r index the individual products in $\mathcal{J}_{ft}$. The price, p_{jt}, and the marginal cost, $\widehat{mc}_{jt}$, for product j must then satisfy the following first-order condition (FOC):

$$s_j(\boldsymbol{p}_t) + \sum_{r \in \mathcal{J}_{ft}} (p_{rt} - \widehat{mc}_{rt}) \frac{\partial s_r(\boldsymbol{p}_t)}{\partial p_{jt}} = 0. \tag{2.7}$$

The J_{ft} equations in (3.13) can be used to calculate the price-cost margins for each product. I define

$$\Omega^{pre}_{jr}(p_t) = \begin{cases} -\partial s_r(\boldsymbol{p}_t)/\partial p_{jt} & \text{if } \exists f : r, j \in \mathcal{J}_{ft} \\ 0 & \text{otherwise} \end{cases} \tag{2.8}$$

and substitute it into the vector form of the FOC to get

$$s(\boldsymbol{p}_t) - \Omega^{pre}(p_t)(p_t - \widehat{mc}_t) = 0.$$

This equation can then be rearranged and used to solve for the markups and the implied marginal costs

$$p_t - \widehat{mc}_t = \Omega^{pre}(p_t)^{-1} s(\boldsymbol{p}_t) \quad \Rightarrow \quad \widehat{mc}_t = p_t - \Omega^{pre}(p_t)^{-1} s(\boldsymbol{p}_t). \tag{2.9}$$

[28] The validity of this assumption is supported by conversations with pharmaceutical industry experts and ample evidence in the relevant literature, which indicate that firms compete by setting prices. In most markets, products are differentiated and firms are not capacity constrained. Additionally, Nevo (2001) found that the Bertrand-Nash equilibrium leads to more accurate predicted margins than other behavioral models. The assumption of a static game does ignore potentially important dynamics that could stem from consumer switching costs, brand loyalty, and advertising. For example, Lu and Comanor (1998) examined pricing strategies by new pharmaceutical entrants and found that high-value drugs were introduced at prices two or three times those of existing drugs, while very similar value drugs entered at similar prices.

Assuming marginal costs are not observed, equation (3.16) allows these values to be calculated using the demand system estimates.[29] This equation can also be used to simulate the equilibrium prices under the modified policy by returning to the previous Bertrand-Nash equilibrium assumption.

2.5 The Estimation

I estimate the parameters of the model presented in the previous section using the data discussed in Section III. I consider each therapeutic class to be a different top-level nest and each molecule to be a bottom-level nest. Thus, the consumer first chooses one of these classes or the outside good, then a molecule from that nest, and finally, a specific product of the molecule.

Observed characteristics include whether the product is a brand or generic, the form of the drug, who produces it, the months in which it was purchased, and how long the molecule has been on the market.

2.5.1 Market Size and the Outside Good

To form my sample, I take the following steps. First, I assign molecules in the SDI database to their corresponding therapeutic classes according to the Anatomical Therapeutic Chemical (ATC) Classification System.[30] Next, I follow the established path of defining daily dose as a common basis of comparison to allow for the estimation of substitutability between products (Stern, 1996b; Berndt et al., 1996; Currie and Park, 2002). I use the *Physicians' Desk Reference* for various years to establish

[29] However, it is important to note that marginal cost estimates rely on the use of consistent demand system estimates. Inconsistent estimates may result in implied marginal costs that appear to jump erratically over time. Additionally, non-negative marginal cost estimates rely on the model correctly capturing firms' profit maximizing behavior.

[30] Established by the World Health Organization Collaborating Centre for Drug Statistics Methodology in 1982, the ATC classifications provide a clear system by which innovating firms can determine to which drug class their innovation corresponds. Moreover, since firms generally sell their pharmaceutical drugs to multiple countries, this international classification system is appropriate.

each molecule's daily maintenance dose levels and divide dose sizes by these corresponding values. These results are then multiplied by the monthly unit sales and divided by the number of days in that month. Third, I calculate the antidepressant market size by multiplying the prevalence rate of depression by both the U.S. Census Bureau's monthly estimates for the civilian population and by the proportion of people that are at least 18 years of age.[31] Fourth, prices are inflated to December 2010 dollars using the Consumer Price Index from the Bureau of Labor Statistics.[32] Finally, for ease of computation, I aggregate the data in two ways. First, I aggregate doses for each brand, manufacturer, and form in a given month. While resulting in a substantial reduction, this step still leaves over 700 brand-manufacturer-form combinations per month. As discussed in Section 2.3.2, I then combine firms that are affiliated through production chains or mergers and end up with 364 products. This last step is particularly relevant to generic drug manufacturers, many of which had merged with or acquired other generic manufacturers. However, the data still includes multiple distinct generic products for each molecule not under patent.

To estimate the relationship between copay and price, I use the MarketScan CCAE Database merged by drug and month with prices from the SDI database. Copay values are taken from the insurer listings that correspond to each patient transaction. I exclude observations in which the corresponding insurer plan requires patients to pay anything other than a copay.[33] The parameters in equation (2.1) are estimated on patients' transaction-level data with prescription-level prices, and weighted by the number of enrollees in each plan. These estimates are then converted to the daily-dose level and incorporated into the demand estimation.

[31] Both the SDI database and the U.S. Census Bureau estimates exclude people who are in the military or are in institutional facilities. (http://www.census.gov/popest/).

[32] The Consumer Price Index can be found at http://www.bls.gov/cpi/.

[33] In the MarketScan CCAE database, some patients are observed to pay other costs, such as co-insurance and a deductible. However, a majority of the observed plans require patients to only pay a copay.

In estimating the demand, I account for both time-varying and time-invariant effects. A number of time-varying product characteristics, (c_{jt},X_{jt},a_{mt}), enter the consumer's utility. Among the X_{jt} characteristics, I first include patent expiration dummies for each molecule to capture any changes in how a product is perceived by consumers. Next, I include time dummies, alone and interacted with a therapeutic class identifier, to capture news that enters the market and affects consumer perceptions. Additionally, I incorporate months-on-market dummies for the first twelve months after a molecule enters the market in order to isolate trends in product availability or consumer awareness and/or learning.[34] These dummies are allowed to vary by therapeutic class. Finally, I include copay at the product level and log advertising at the manufacturer-molecule-month level. This paper treats advertising as exogenous. Pharmaceutical firms typically lay out their advertising schedules far in advance and these expenditures do not appear sensitive to monthly demand shocks that are commonly absorbed into the error term. Furthermore, I do not attempt to solve for new advertising levels in the counterfactuals, but I do exclude advertising for products that have been removed from the market. The time-invariant characteristics are captured by molecule-level and manufacturer-form-level fixed effects. The distinction is necessary due to the nesting structure of the model.

Following Nevo (2003), I make two important assumptions relevant to the interpretation of the counterfactual results. First, I assume that the quality of the outside option (possibly, therapy or nothing) does not decrease over time.[35] Second, I assume that any changes in consumers' perceived value of a product's unobserved characteristics primarily stem from changes of those characteristics that happen over time. Hence, ξ_{jt} is allowed to vary over time in the welfare calculation.

[34] For robustness, I included longer periods of time and found no meaningful variation.

[35] This assumption was included after conversations with several industry experts and medical practitioners.

2.5.2 Instruments

Following Stern (1996a,b), I instrument for product prices and the potential endogeneity of the within-nest shares using supply-side factors. These instruments are intended to be unrelated to the unobserved heterogeneity (possibly quality), but are systematically correlated with pricing decisions and the determinants that affect within-group share. The first set of instruments are those based on the amount of competition within a nest. For a given product, I count the total number of other products in the nest that are generics, the percentage of those other products that are generics, and the number of other firms that sell products in the nest.[36] These three simple measures capture the degree of competition a given product faces, but should not be related to unobserved quality. Also, I can use the total sum of time since entry of other products in the nest as an instrument. The FDA imposes strict regulations on the drugs sold on market and all changes to an approved product must also be approved. Hence, controlling for a product's own time on market, the aggregate time since entry of all other products will not be related to a given product's unobserved quality.

As noted by Stern (1996a,b), multi-product market power is also likely to influence prices, but not unobserved quality. To that end, the second set of instruments I employ are the numbers of other products sold by a given product firm in each nest. Since firms are assumed to maximize profits over their entire product portfolio, changes to the portfolio will affect the prices it sets, but not the unobserved quality of a given product.

[36] One concern raised by Ellison et al. (1997) to the use of the number of firms as an instrument is that firms could be entering or exiting a market in response to changing demand characteristics. While this is a valid concern, I do not find a great deal of this type of movement by firms in the data. I observe a great deal of entry, but not as much exiting. Further, it is rare to see a product enter the market, leave, and then re-enter.

2.6 Estimation Results

In this section, I review the estimates of the model and compare them to findings in other papers. I start with the copay-price relationship defined in equation (2.1), which is estimated by nonlinear least squares regression. As expected, Table 2.2 shows a positive relationship between copay and price. More specifically, a one percent increase in the price of product j results in roughly a 0.42% increase in the copay for that product.

The copay regression results allow me to estimate demand based on the costs that patients observe. Table 2.3 provides the key demand-side parameter estimates. The nest parameters imply that the therapeutic class designation is meaningful. That is, products in the same therapeutic class are considered better substitutes and so, consumers are less likely to switch to other product classes. Given that a molecule belongs to only one therapeutic class, the second parameter will be larger by construction. However, there is still some meaningful distinction between molecules.[37] The estimated parameters on the fixed effects are also meaningful. The months-on-market parameters show that the SSRI class were slow to gain traction in the first couple of months, but resembled the other drugs on market soon after.

Own-price and cross-price elasticities provide additional insight into how a change to patent policy will affect a market.[38] Using the demand estimates, I calculate the own-price elasticities to range between -1.6 and -3.2 for the two dominant therapeutic classes, shown in Table 2.4. The average cross-molecule elasticities for the SSRI class, which are presented in the last four rows of the last column, are quite large. These imply that blocking one of these products from the market will have a substantial positive impact on the market shares of the other SSRI products. Alternatively,

[37] Omitting the class-level nests and estimating demand as a simple nested logit with molecule-level nests, yields an estimate of similar magnitude to the coefficient for $\ln(s_{jt/m_g})$.

[38] I provide the derivation of these elasticities in Appendix A.

the cross-class price elasticities in the first four rows of the last column are relatively small. This implies that if an SSRI product is blocked from the market, consumers are not very likely to switch to an NGA product. Additionally, any product blocked from the NGA class would have an even lower impact on the SSRI products. These results indicate that substitutability within a given drug class is quite high, which suggests that extending patent breadth from the molecule level to the therapeutic class may be welfare improving. Beyond that, the products are sufficiently differentiated that extending breadth to the full market would most likely have a negative impact on both producers and consumers by comparison.

A few other papers have examined the antidepressant market with mixed results. Mortimer (1998) used three years of data from the early 1990's to estimate own-price elasticities for branded drugs in this market range between -1.9 and -1.1, but with small cross-price elasticities. Alternatively, Cleanthous (2002) used annual data and found own-price elasticities between -0.54 and -0.02, and similiarly small cross-price effects. Both Mortimer (1998) and Cleanthous (2002) rely on average retail prices rather than copays in their demand estimation which may explain why they found consumers to be less price sensitive. Finally, Dickstein (2011) employed a dynamic learning model on patient-level claims data and reported own-price elasticities that range between -0.9 to -0.24.

2.7 Modified Policies

This section provides a framework that measures the welfare implications of modifying patent breadth and length, which is then applied to the pharmaceutical industry. As suggested by the theory, I utilize my estimates of consumers' substitution behavior as well as features of the market to inform my analysis.

2.7.1 Overview

An empirical assessment of the trade-offs between patent breadth and length is motivated by two key factors. The first is that this assessment would better inform the theory and provide additional insight to policymakers. While some of the prior applied literature has attempted to provide insights through indirect analysis, this paper is the first to directly examine this trade-off. The other key factor is the debate on the value of "me-too" drugs. This paper provides an approach that allows for a more reasonable comparison of the value of these products to the potential value of ealier generic entry on high-quality drugs. The approach is also extended to consider the incentives of "me-too" innovators to provide more accurate welfare calculation.

The abstract search for an optimal patent policy is limited to what is feasible for a given market. As previously mentioned, any analysis that searches for an optimal patent policy requires that the measure of patent breadth be defined in such a way that is known to the market and independent of any decisions made by the firms. For the pharmaceutical industry, there are three such feasible levels for breadth. The narrowest is the molecule level, which is the breadth specified under the existing policy. The other two are the therapeutic class level and the entire market. I expand breadth to the therapeutic class and then scale the patent length in order to make the high-value innovator indifferent between the two policies.[39]

For my policy experiments, I model patent breadth on the high-value innovation as the degree to which it can restrict "me-too" products from entering the market.[40] Moreover, I allow those "me-too" innovators that are restricted from the market to keep their patents under the modified policy.[41] The implication of this is that once

[39] This follows the conceptual framework in much of the prior literature.

[40] As discussed in Section 2.3.1, the temporal disconnect between when an innovation is patented and when its value is known implies that the conventional framework of patent policy is not well suited for examining alternative levels of patent breadth and length.

[41] This paper focuses on only one market. In footnote 15, I discuss how the framework can be

the patent on the high-value product expires, the "me-too" products can then enter the market.

For the purpose of exposition, Figure 2.5 depicts the profit over time for both a high-value innovation, m_0, and a subsequent "me-too" innovation, m_1. Upon its entry, m_1 negatively impacts the profit of m_0. I propose a policy modification whereby m_0's patent breadth is increased so as to exclude m_1 from the market, while simultaneously limiting its patent life to ensure at least the same net present discounted profit earned under patent protection, V^f. Figure 2.6 portrays this balance with the shaded regions, which are equivalent in present discounted value. In practice, m_0's net present discounted profit under patent protection may be greater than V^f if time is treated as a discrete measure. As previously mentioned, the market exclusion restriction on m_1 expires with m_0's patent.

I focus my analysis on the market for antidepressants, in which Prozac was the first SSRI and was clearly a high-value innovation. Given that there is no formal definition or explicit quality threshholds that distinguish high-value and "me-too" innovations, I assume that the four SSRI products that enter the market after Prozac are "me-too"s. Note that this assumption is independent of how consumers may view these products.[42] I extend Prozac's patent breadth to the therapeutic class level and temporarily exclude these "me-too" innovations. This restriction only applies to subsequent entrants in the SSRI class and therefore, innovations in other classes would not be directly affected.

Below, I present two counterfactuals. The first assumes that all "me-too" innovations that entered under the original policy also enter under the modified policy, once Prozac's shortened patent length expires. For the second counterfactual, I provide a

adapted to allow for products that compete in multiple markets.

[42] Ongoing work relaxes this assumption and allows for the consideration that these subsequent products may themselves be high-value innovations.

framework which allows "me-too" innovators to anticipate the impact of the modified policy and re-optimize their entry decision before entering Phase III clinical trials. Innovators that choose to forgo additional drug development and eventual market entry would save the associated investment costs.

2.7.2 Counterfactual Pricing

Under the counterfactuals, equilibrium prices are determined for the set of products on the market in each period. To do so, the implied marginal costs under the current policy are assumed to remain the same under the counterfactual policy. I define the matrix Ω^{post} according to equation (3.14) under the modified policy. The predicted equilibrium price, p_t^*, under the modified policy solves

$$p_t^* = \widehat{mc_t} + \Omega^{post}(p_t^*)^{-1}s(\boldsymbol{p}_t^*) \tag{2.10}$$

where $\widehat{mc_t}$ is the implied value calculated from equation (3.16). This equation entails a couple of nontrivial assumptions in addition to the Bertrand-Nash equilibrium. First, I assume that the cost structure between the two policies remains the same. Second, the matricies Ω^{pre} and Ω^{post} are assumed to rely on the same demand estimates. Hence, the alternate market structure and resulting price differences for the remaining products are assumed to capture all the differences between the two systems. This implies that firms do not change their strategies in any other dimensions that may affect demand.[43]

2.7.3 Exogenous Entry

Social Welfare under Exogenous Entry

The net discounted social welfare impact of the modified policy is the sum of the discounted effects on consumers (CV), insurers (Π^{ins}), and producers (Π^{diff}).[44] This

[43] As previously discussed, advertising is held fixed.

[44] Producers include both innovators and manufacturers.

is given by

$$SC = CV + \Pi^{ins} + \Pi^{diff}. \tag{2.11}$$

I assume that consumers and insurers have an annual discount rate of 5% while the producers' discount rate is 11%, which accounts for the innovator's risk of product failure during the product development process (DiMasi et al., 2003). The use of this higher producer discount rate means that, for a given amount of patent breadth, the innovator of the groundbreaking drug will require relatively less patent length in order to realize V^f. Under exogenous entry, consumers benefit from this shortened patent length due to the expedited entry of the generics on Prozac's molecule.[45] The implications for the "me-too" innovators is less clear. While they are able to enter the market sooner under the higher discount rate, they also place greater value on the time they are restricted from the market. However, I find that the final results are not qualitatively different when I use a 5% discount rate for producers.

As previously noted, prescription drug costs comprise only a small fraction of household income. Thus, I use compensating variation to calculate the impact that switching to the modified patent policy will have on consumers. Interestingly, this impact can be fully captured by the difference in log shares of the outside good under the two policies, magnified by the size of the market and translated into dollars by the disutility of price (copay) (Arcidiacono and Miller, 2011). For all consumers at time t, this is given by

$$CV_t = -\frac{M_t}{\alpha}\left[\ln\left(s_{0t}^{ante}\right) - \ln\left(s_{0t}^{post}\right)\right] \tag{2.12}$$

where s_{0t}^{ante} and s_{0t}^{post} denote the share of the outside good at time t under the current

[45] In the case of endogenous entry, consumer welfare will depend on the choices made by the "me-too" innovators.

and modified policies, respectively. The total discounted welfare change is then

$$CV = \sum_{t=1}^{T} CV_t \cdot (1 - d^c)^{t-1} \tag{2.13}$$

where d^c is the rate at which consumers discount utility.

While consumers pay only a fraction of the full drug prices, the rest of the price is paid by insurers. Therefore, insurer savings from the switch to the modified policy is given by

$$\Pi^{ins} = \sum_{t=1}^{T} \left\{ \sum_{j=1}^{J} \left[(p_{jt}^{ante} - c_{jt}^{ante}) s_{jt}^{ante} - (p_{jt}^{post} - c_{jt}^{post}) s_{jt}^{post} \right] \cdot M_t \cdot (1 - d^c)^{t-1} \right\}, \tag{2.14}$$

where the terms identified as *ante* and *post* correspond to the equilibrium prices and shares under the current and modified policies, respectively. Note that the insurers, like the consumers, are payers and so their expenditures are discounted by the consumer rate, d^c.

For the producers' net total welfare effect (innovators and generic manufacturers), the difference of each producer's profit under the current and modified policies is summed across all producers and discounted to time $t = 1$. That is,

$$\Pi^{diff} = \sum_{t=1}^{T} \left[\sum_{f=1}^{F} \left(\Pi_{ft}^{post} - \Pi_{ft}^{ante} \right) \cdot (1 - d^f)^{t-1} \right], \tag{2.15}$$

where d^f is the rate at which producers discount profits, and Π_{ft}^{ante} and Π_{ft}^{post} are producer f's profit (calculated according to equation (4.5)) under the current and modifed policies, respectively.

For simplicity in implementing the simulations of the modified patent policies, I use the averages over time of both implied marginal cost, mc_j, and unobserved product heterogeneity, ξ_j, for each product j.

Results under Exogenous Entry

Prozac entered the antidepressant market in January 1988 and its patent expired in July 2001. This means that Prozac enjoyed an effective patent life of 13.5 years. During its patent-protected time on market, three other SSRI drugs entered the market: Zoloft, Paxil, and Celexa. I assume that these are "me-too" drugs, and restrict them from the market until Prozac's patent expires under the modified policy. Under the original policy, I then calculate the present discounted profits generated by Prozac while under patent protection. This amount is then set as the minimum profit requirement under the modified policy. Given the restriction under the modified policy, I find that Prozac's innovator, Eli Lilly, is able to earn at least the same present discounted profits with a patent that expires in September 1995.[46] This is a difference of nearly six years (70 months) or a 43% reduction in Prozac's effective patent life.

The impact of the policy switch on the "me-too"s is shown in Table 4.2. The effective patent life for Zoloft and Paxil is shortened by 3.58 years and 2.67 years, respectively. This is roughly a 25% reduction in the patent protected time on market for both drugs.[47] On the other hand, Celexa entered the market in August 1998 and so its effective patent life is unaffected. Once on the market, the "me-too" drugs compete against both Prozac and its generic variants (fluoxetine). Discounted to January 1991, Zoloft experienced a $2.9 billion loss in profit (63% reduction) due to its delayed entry and competition against generic fluoxetine. For Paxil, this loss was only $621 million, but this amounts to more than 75% of its profit under the original policy. The impact on Celexa is exclusively from its competition with generic fluoxetine. The last row in Table 4.2 shows the impact of the generic versions of each

[46] Note that time in my data is in increments of months.

[47] While Paxil entered the market several months after Zoloft, its patent expired nearly four years before Zoloft's. See Table 4.1.

of these "me-too" drugs, which are fairly insignificant, amounting to less than 1% of their respective profits.

Table 4.3 provides the total effect for each segment of the market. Under the counterfactual simulation, Prozac earned an additional $16 million, primarily due to the discreteness of time in setting the new patent length. The impact of the policy switch generated more than $4 billion in additional profits for producers of generic fluoxetine. Note that I assume that the number and relative timing of entry among the generic fluoxetine producers remains the same. The overall timing is simply advanced to the new patent expiration date for Prozac.[48] Additionally, the generic products are differentiated products on the market and generally price above marginal cost. The total impact for "me-too" brands and generics are simply the totals of the figures in Table 4.2. As expected, the impact on the rest of the products in the market is nearly insignificant. Interestingly, the net impact across all producers is a gain of only $36 million. Allowing additional generic entry on fluoxetine would then reduce their super-normal profits and lead to a large and negative net impact across all producers. However, this potential negative impact on producers is overshadowed by the substantial savings by insurers, more than $10.2 billion (a 14.4% reduction in expenditures). This is due to the substantially lower cost to insurers when consumers purchase generics over brand name products and with the advanced timing of generic entry on Prozac. Finally, this advanced timing of generic entry also results in a small net gain to consumers, despite the broadening of Prozac's market exclusivity to temporarily restrict the entry of "me-too"s. The overall effect on social welfare is a $10.5 billion gain.

The above policy experiment addresses the current debate in the pharmaceutical

[48] For example, consider two generic firms, A and B, where Firm A enters two months before Firm B. Under the counterfactual, Firm A will still enter two months before Firm B, even though overall both enter the market earlier.

literature on limiting the incentives of "me-too" drugs. This is achieved by modifying the patent breadth and length of the high-value innovation and maintaining the same entry decisions for subsequent entrants. For the second policy experiment, I relax this assumption on the entry decisions by "me-too" innovators. This provides a more robust approach to estimate the social welfare impact.

2.7.4 Endogenous Entry

Entry Re-optimization

I now consider the impact of allowing "me-too" innovators to re-optimize their decision to enter Phase III clinical trials under the modified policy.[49] I implement this by focusing on innovators that were observed to enter the market under the current policy and comparing their entry costs to their expected profits. Hence, an innovator will save its investment costs of Phase III if it chooses not to continue. For simplicity, I assume that entry of previously unseen products does not occur under the modified policy. Under the current policy, innovators enter in a sequential order $f^1, ..., f^n$ and then realize profits $\Pi^{1,ante}, ..., \Pi^{n,ante}$, respectively. It is also assumed that this order reflects the order in which innovators reach their decision point at the end of Phase II clinical trials. Finally, I assume a full information game where innovators see the product qualities, development costs, and time to market entry of all the other potential market entrants. Therefore, innovator f can anticipate the impact of the modified policy on the timing of when product j would be allowed to enter the market.

Let $\mathfrak{C}_{fj}$ be innovator f's fixed Phase III clinical trial costs for product j and assume $\mathfrak{C}_{fj} \sim \mathcal{F}_N(\mu, \sigma^2 | 0 \leqslant \kappa < \mathfrak{C}_{fj} < V_{fj}^{ante})$, where $\mathfrak{C}_{fj}$ is independent across innovators and products, V_{fj}^{ante} is innovator f's net present discounted profit from

[49] As discussed in Section 2.3.1, innovators gain significant information on the safety and efficacy of their innovations during Phase II of clinical trials. I assume that this is sufficient to make an informed decision.

product j under the current policy, κ is a lower bound on costs, and $\mathcal{F}_N$ is a truncated normal distribution:

$$\mathcal{F}_N = \frac{\Phi(\frac{\mathfrak{C}_{fj}-\mu}{\sigma}) - \Phi(\frac{\kappa-\mu}{\sigma})}{\Phi(\frac{V_{fj}^{ante}-\mu}{\sigma}) - \Phi(\frac{\kappa-\mu}{\sigma})}. \tag{2.16}$$

Innovator f will choose to send product j to Phase III clinical trials under the modified policy if $\mathfrak{C}_{fj} < V_{fj}^{post}$, where V_{fj}^{post} is innovator f's net present discounted profit from product j under the modified policy.[50]

In order to estimate the probability of each possible market outcome under the modified policy, I apply the following simple algorithm:

1. Draw $\mathfrak{C}_{fj}$ for each product.

2. Determine the re-optimized decision for each product using backward induction.

3. Repeat Steps 1 and 2 $\mathcal{N}$ times.

4. Finally, calculate λ_n, the probability of each possible market outcome, $n = 1, ..., N$.

When simulating the entry re-optimization, I use estimates (in December 2010 dollars) calculated by DiMasi et al. (2003) for average Phase III costs, μ = \$143 million, and standard deviations, σ = \$118 million, for approved drugs. DiMasi et al. (2003) also estimated that the average length of time from the start of Phase III to drug approval is 52 months. I use this estimate to calculate V_{fj} for innovator f and product j. Finally, I set κ to be \$1 million.

Social Welfare under Endogenous Entry

The social welfare calculation under endogenous entry is a simple analog of the exogenous case that includes probability weights for the N market outcomes. The

[50] Given that these products were approved by the FDA under the current policy, they would still be approved under the modified policy. The question is merely one of timing if products continue on to Phase III.

equations corresponding to (4.2)-(4.6) for the counterfactual with endogenous entry for "me-too"s are given by:

$$CV_{t,n} = -\frac{M_t}{\alpha}\left[\ln\left(s_{0t}^{ante}\right) - \ln\left(s_{0tn}^{post}\right)\right], \tag{2.17}$$

$$CV = \sum_{n=1}^{N} \lambda_n \left[\sum_{t=1}^{T} CV_{t,n} \cdot (1-d^c)^{t-1}\right], \tag{2.18}$$

$$\Pi^{ins} = \sum_{n=1}^{N} \lambda_n \left(\sum_{t=1}^{T}\left\{\sum_{j=1}^{J}\left[\left(p_{jt}^{ante} - c_{jt}^{ante}\right) s_{jt}^{ante} - \left(p_{jtn}^{post} - c_{jtn}^{post}\right) s_{jtn}^{post}\right] \cdot M_t \cdot (1-d^c)^{t-1}\right\}\right), \tag{2.19}$$

$$\text{and} \quad \Pi^{diff} = \sum_{n=1}^{N} \lambda_n \left\{\sum_{t=1}^{T}\left[\sum_{f=1}^{F}\left(\Pi_{ftn}^{post} - \Pi_{ft}^{ante}\right) \cdot (1-d^f)^{t-1}\right]\right\}. \tag{2.20}$$

Let $I_{jn}^{PhaseIII}$ be the expenditure saved when innovation j is abandoned rather than taken to Phase III clinical trials, discounted to time $t = 1$ using the rate d^f. The total expenditure saved across all such abandoned innovations is given by

$$I^{PhaseIII} = \sum_{n=1}^{N} \lambda_n \left(\sum_{j=1}^{J} I_{jn}^{PhaseIII}\right). \tag{2.21}$$

Finally, the discounted social welfare effect is then given by

$$SC = CV + \Pi^{ins} + \Pi^{diff} + I^{PhaseIII}. \tag{2.22}$$

Results under Endogenous Entry

As before, the "me-too" drugs may enter the market starting in September 1995. The first two rows of Table 4.4 provide the lower and upper bound values that plugged into the truncated normal distribution in equation (4.7). To calculate the upper bound, the net present profit of each product is discounted back to the start of Phase III clinical trials. This is assumed to be 52 months prior to the orginal market

entry date for all products. Note that all of the products have an upper bound that is substantially higher than the distribution mean of $143 million. The average and standard deviation of draws from step (1) of the algorithm are given in the middle two rows of Table 4.4. Given that the "me-too" innovators make their decisions in sequential order, backward induction is used to determine the market outcome for each set of cost draws. The probability of entry for each drug is provided in the fifth row of the table. Zoloft will always go into Phase III clinical trials and eventually enter the market, while Celexa and Paxil will do so 88% and 48.5% of the time, respectively. The saved expenditure weighted by market outcome is given in the last row of the table.

The impact of the policy switch on the "me-too"s is shown in Table 4.5. The first row matches the results in the first row of Table 4.2. Intuitively, it is expected that profit loss for the "me-too" brands would be lower, given the ability to reoptimize the entry decision. This can be seen by summing the saved expenditure and the change in product profit. The impact on the "me-too" generics is more dependent on the entry decisions by the corresponding innovators. If a brand product is abandoned by its innovator, generic entry on that molecule is assumed to never occur. Interestingly, while generics of Paxil experience substantial losses, those on Zoloft actually benefit. This is likely due to the reduced level of competition when generic versions of Paxil do not enter the market.

The net welfare effect for each segment of the market is provided in Table 4.6. This time, the impact on generic versions of Prozac is larger due to the limited competition when the other "me-too" products are abandoned. The fourth and fifth rows of the table show that the other products on the market also enjoy this benefit. Overall, the producers gain nearly $149 million in direct profit. By abandoning their products, these innovators also saved $127 million in Phase III expenditures. Not surprisingly, insurer saving are also larger under the modified policy with endogenous

entry, reflecting the higher consumption of generic fluoxetine. The consumers welfare calculation shows that consumers still prefer the modified policy, but that their benefit is tempered by the decrease in products variety on the market. Overall, the social welfare gain is nearly $11.4 billion, which is larger than the modified policy with exogenous entry.

2.8 Conclusion

This paper provides the first empirical assessment of the trade-off between patent breadth and patent length. I draw on key insights from the theoretical literature, which highlights the importance of the market structure and shape of the demand curve in determining optimal patent policy. I first estimate demand parameters to determine insured consumers' product substitution patterns. Incorporating the estimated demand parameters into a model of supply, I then back out firms' marginal costs of production, allowing me to perform counterfactual analyses. I use 20 years of retail prescription sales data on the market for antidepressants along with advertising, targeted to physicians and nurses, for each drug. Demand estimates indicate that consumers consider products within each therapeutic class to be much closer substitutes than those across classes.

Using estimates from the static models of demand and supply, I consider two policy simulations. The first modifies the patent of the first-in-class groundbreaking drugs to address the debate in the pharmaceutical policy literature on the value of limiting the development of "me-too" drugs. Specifically, I expand the patent breadth and limit the patent length of the groundbreaking antidepressant drug, Prozac, in order to temporarily restrict the subsequent "me-too" products from entering the market. Estimates show that under this modified policy, Prozac is able to generate equivalent net present discounted profit under patent protection with an effective patent length that is 43% shorter than under the original policy. Assuming all "me-

too" products eventually enter the market, I find small welfare gains for producers and consumers along with substantial gains to insurers in the form of expenditure savings. Even if gains by manufacturers of generic Prozac (fluoxetine) were ignored, the net social effect is still positive.

The second policy simulation extends the first, by allowing the "me-too" innovators to anticipate the impact of the modified policy and reoptimize their entry decisions during their respective drug development processes. Those innovators that abandoned their drugs save their remaining investment expenditures. Through simulations, I find that while Zoloft would always proceed through Phase III clinical trials and onto the market, Paxil and Celexa would only do so with probabilities of 48.5% and 88%, respectively. As expected, producers' welfare improves with their ability to reoptimize their entry decisions. In cases where the products do not enter the market, consumers lose the value of "me-too" entry as well as the generics that would have followed on each molecule. However, this loss is still overshadowed by the gain of earlier generic entry on fluoxetine. Insurers now realize even greater gains as consumers who would have otherwise purchased Paxil and Celexa, turn to generic fluoxetine instead.

My results indicate the potential for meaningful social gains from exploring modified patent policies. A weakness is that while the assumptions simplify the problem, some also limit the generalizability of my conclusions. For example, I abstract away from any uncertainty consumers may have of the quality of new products introductions. If consumers learn about this quality from each other, then the higher counterfactual price on Prozac would induce more price-sensitive consumers to switch to generic versions. In turn, this would speed up consumers' learning process as well as the adoption rate of these generics. Therefore, the modified patent policy could potentially further increase the competitive pressure on Prozac's innovator after patent expiration. A second example is that it is unlikely that insights from this

analysis can be extended to the biologics (large molecules) segment of the industry, given that their innovation and patenting is conducted differently. However, the policy framework may be applicable to other industries like chemicals and agriculture, where innovation costs may be high relative to imitation costs, and secrecy provides insufficient protection due to the possibility of reverse engineering.

To allow for a more robust policy framework, many of these assumptions can be relaxed. Chief among these is the assumption that all products that follow the first-in-class drug provide only an incremental benefit. Ongoing research allows the FDA (or another independent agency) to formalize the distinction between high-value and "me-too" drugs according to a clearly defined margin of value. Thus, high-value innovators that may be second-in-class or later observe clear guidelines necessary to enter the market without additional delay. To limit the inherent risk for products that are in close competition to be first-in-class, a compromise may allow the second innovator to enter the market without delay if it reaches the FDA review within some period of time after the first-in-class molecule (Hollis, 2004). It is left for future work to examine the effects of relaxing other assumptions, including those restricting the dynamic behavior of insurers and other market participants.

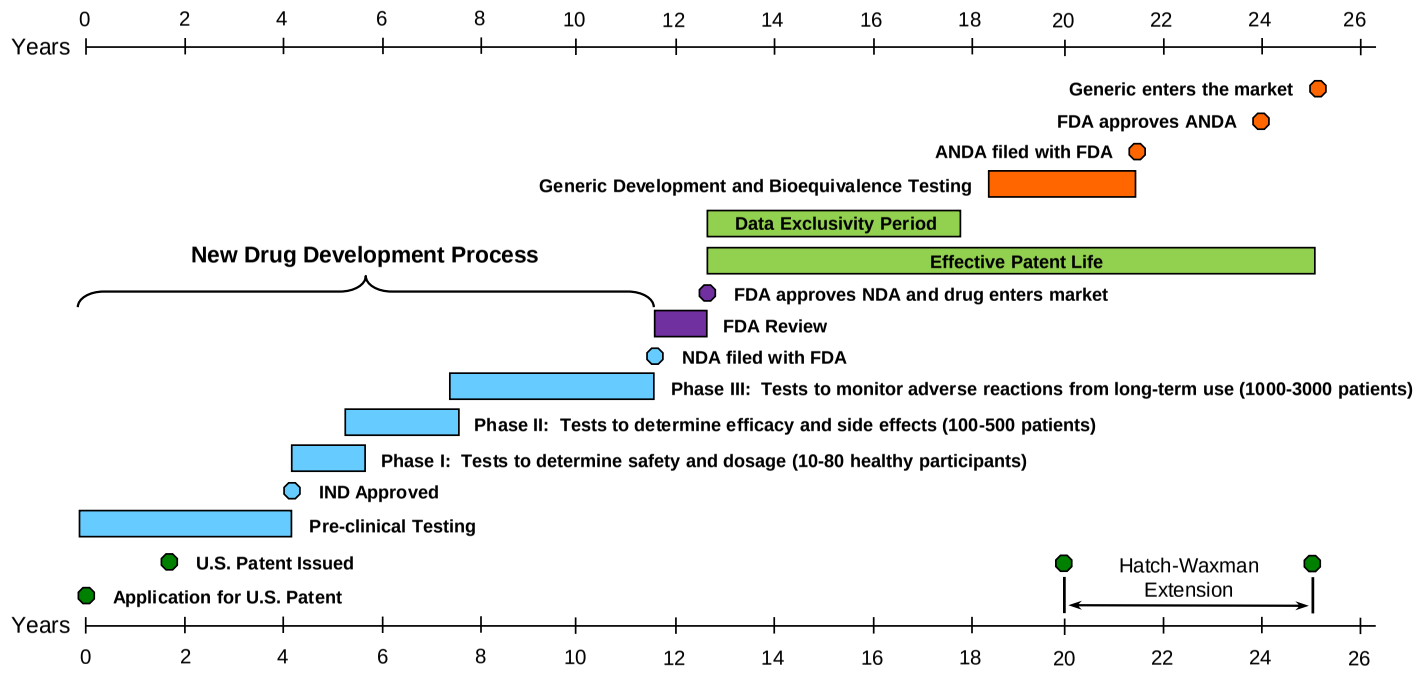


FIGURE 2.1: Drug Development Time Line: Adapted from the time-line figure in Mossinghoff (1999)

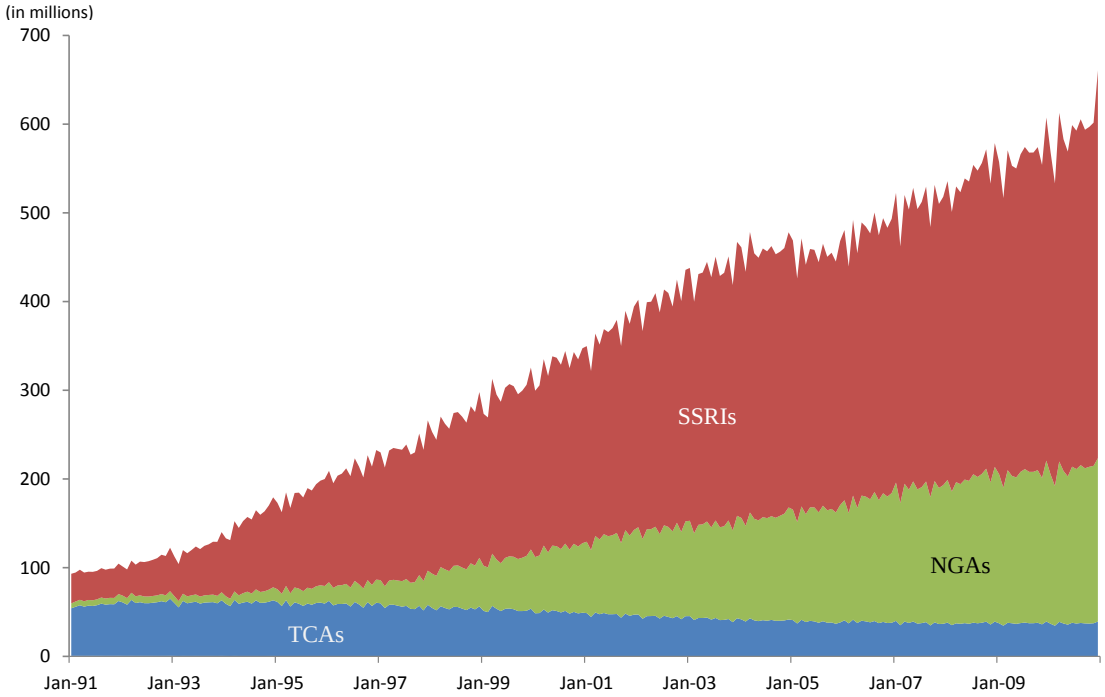


FIGURE 2.2: Area Plot of Monthly Quantity Sales by Therapeutic Class with Standardized Daily Doses: January 1991 – December 2010

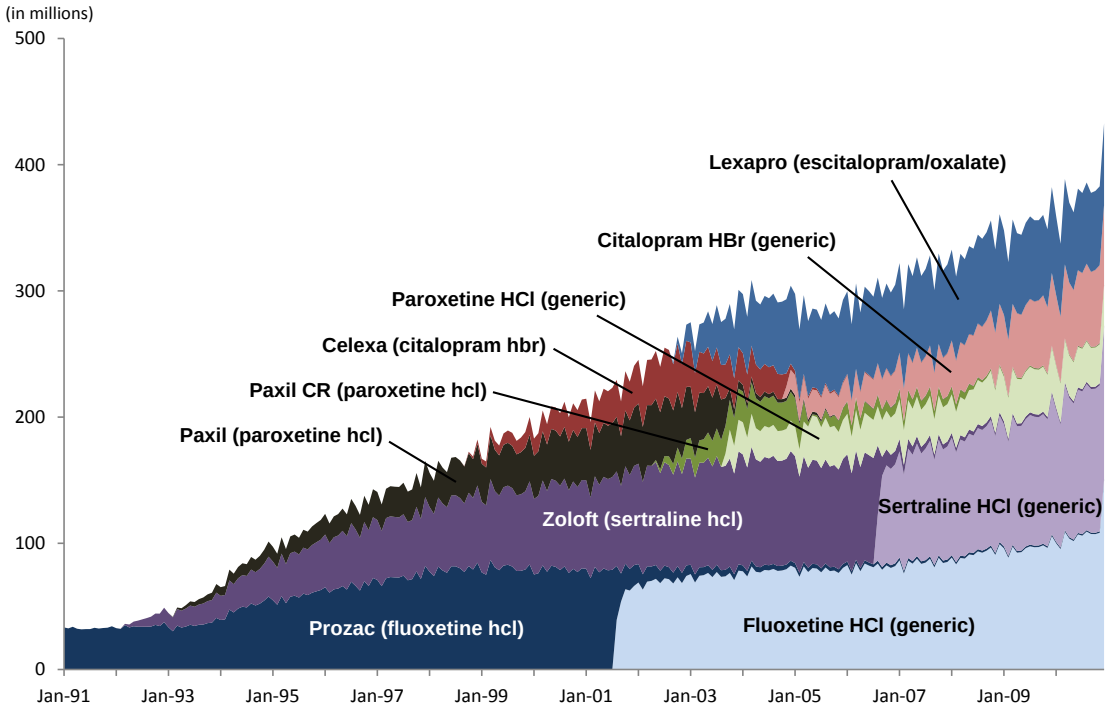


FIGURE 2.3: Area Plot of Monthly Quatity Sales for the Top SSRI Molecules with Standardized Daily Doses: January 1991 – December 2010

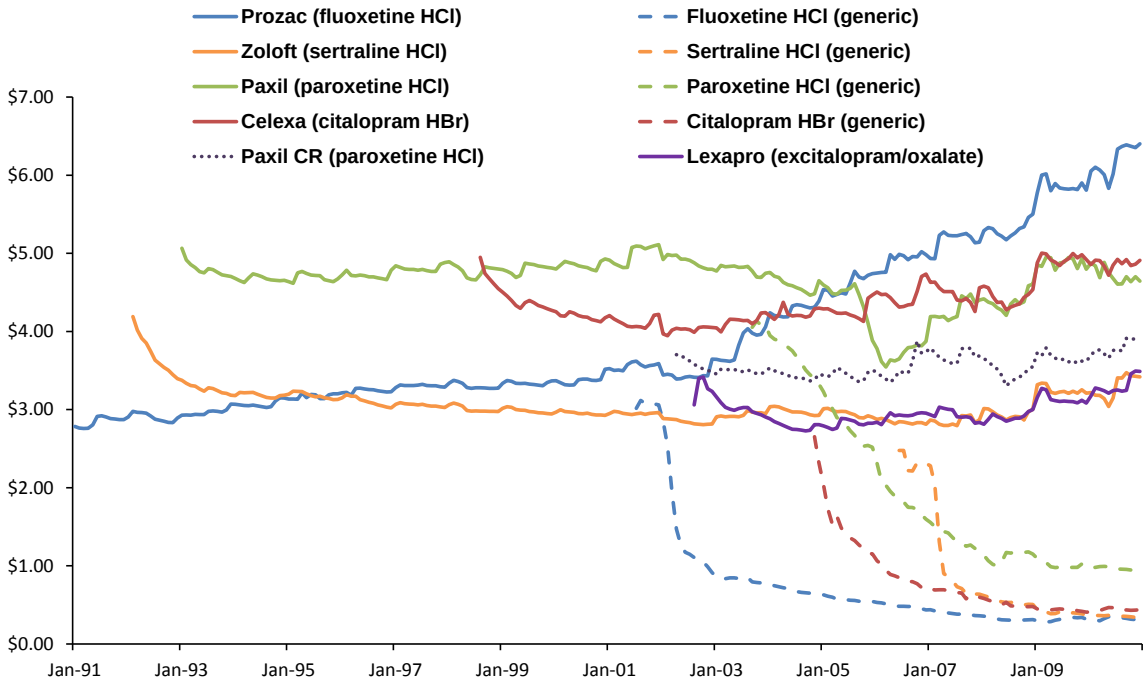


FIGURE 2.4: Prices for the Top SSRI Molecules (in 2010 dollars) Standardized to Daily Doses: January 1991 – December 2010

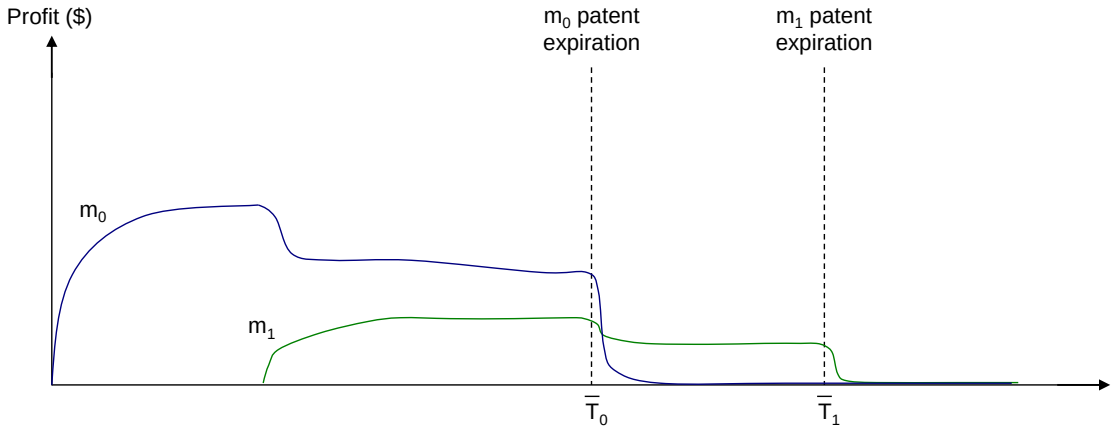


FIGURE 2.5: Demonstrative for Current Patent Policy

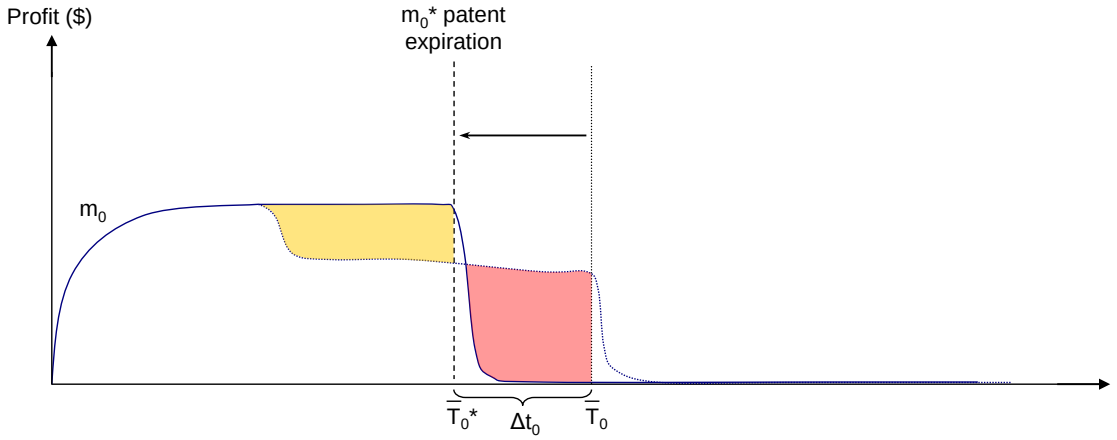


FIGURE 2.6: Demonstrative for Modified Patent Policy

Table 2.1: Drug Details and Summary Statistics

Drug Characteristics						**Prescription Prices ($)**					
						Brands			**Generics**		
Drug Class	Molecule[a]	1^{st} Brandname	1^{st} Launch	1^{st} Patent Exp.[b]	Number of Generics[c]	Retail[d]	Patient Copay[e]	Insurer[f]	Retail[d]	Patient Copay[e]	Insurer[f]
NGA	bupropion	Wellbutrin	1986m3	1999m12	8	166.35	24.71	141.64	86.84	9.45	77.39
NGA	venlafaxine	Effexor	1994m2	2006m8	14	153.60	21.67	131.93	96.86	7.54	89.32
NGA	nefazodone	Serzone	1995m1	2003m9	7	144.38	17.02	127.36	61.54	8.64	52.90
NGA	mirtazapine	Remeron	1996m7	2003m1	11	106.84	21.39	85.44	36.44	8.66	27.77
NGA	duloxetine	Cymbalta	2004m8	–	–	147.53	29.19	118.35	–	–	–
SSRI	fluoxetine	Prozac	1988m1	2001m7	18	130.66	25.86	104.80	14.44	9.58	4.86
SSRI	sertraline	Zoloft	1992m2	2006m6	17	88.32	21.38	66.95	12.85	8.31	4.54
SSRI	paroxetine	Paxil	1993m1	2003m5	9	123.15	22.39	100.75	44.15	9.29	34.85
SSRI	citalopram	Celexa	1998m8	2004m10	17	130.35	26.92	103.43	16.71	8.78	7.94
SSRI	escitalopram/oxalate	Lexapro	2002m8	–	–	88.24	27.97	60.27	–	–	–

Source: SDI Database and MarketScan Commercial Claims and Encounters Database, years 1996-2009.
[a] Selected sample of the top selling antidepressants.
[b] First patent expiration values are missing if the patents are still active on December 2010.
[c] Generics refers to the number of generic producers that compete under a given molecule.
[d] Values of retail prices reflect the mean across the market prices corresponding to each patient record. Based on 124,380 patient records.
[e] Values of copayments reflect the mean across 876 plans in the data. Each plan sets distinct copayments.
[f] Insurer expenditures are the difference between the retail price and the patient copay.

Table 2.2: Copay Regression[a]

Regressor	Coefficient	Std. Err.
ϕ	0.4277	(0.0189)
brand (binary)	0.5885	(0.0135)
γ_0	0.3607	(0.0795)

[a] Dependent variable is c_{jt}. Estimated at the patient-prescription-month level. Based on 194,367 observations. Copays are taken from insurance plan listings. Heteroskedasticity-robust standard errors are reported.

Table 2.3: IV Regression Results [a]

Regressor	Coefficient	Std. Err.	Coefficient	Std. Err.	1^{st} Stage F-Stat.
nest parameters					
ln(molec. share of class)	0.5574	(0.0295)			70.1
ln(prod. share of molec.)	0.6504	(0.0238)			77.6
copay	-4.5683	(0.3591)			127.7
ln(detailing)	0.0582	(0.0095)			
brand (binary)	2.8652	(0.2016)			
Months on Mkt			*Interacted w/ SSRI*		
Month 1	-0.4817	(0.6365)	-2.6344	(0.6699)	
Month 2	-0.4716	(0.6338)	-1.2171	(0.6489)	
Month 3	-0.4673	(0.6442)	-0.7420	(0.6570)	
Month 4	-0.4693	(0.6441)	-0.5286	(0.6540)	
Month 5	-0.4582	(0.6561)	-0.4075	(0.6645)	
Month 6	-0.4916	(0.6325)	-0.3018	(0.6407)	
Month 7	-0.4788	(0.6271)	-0.5409	(0.6471)	
Month 8	-0.4782	(0.6340)	-0.3543	(0.6415)	
Month 9	-0.5260	(0.6079)	-0.2320	(0.6138)	
Month 10	-0.5061	(0.6230)	-0.1852	(0.6275)	
Month 11	-0.4738	(0.6310)	-0.1679	(0.6348)	
Month 12	-0.6328	(0.4272)	0.0245	(0.4338)	

[a] Dependent variable is $\ln(s_{jt}) - \ln(s_{0t})$. Based on 31,872 observations. All standard errors are clustered at the quarter-molecule level.

Table 2.4: Price Elasticities: January 1995

Class	Molecule	Own-Price Elasticity	NGA	SSRI
NGA	bupropion hcl	-2.4468	0.2602	0.0722
NGA	nefazodone hcl	-3.1590	0.2756	0.0722
NGA	trazodone hcl	-1.6101	0.4183	0.0722
NGA	venlafaxine hcl	-2.4716	0.1927	0.0722
SSRI	fluoxetine hcl	-1.7482	0.0045	0.4385
SSRI	paroxetine hcl	-2.9028	0.0045	0.7780
SSRI	sertraline hcl	-2.1597	0.0045	0.8006

[a] *Source:* SDI Monthly Data over the period 1991 to December 2010. The elasticity in the ith row and jth column is the average demand elasticity across products in molecule i with respect to the price of products in nest j.

Table 2.5: Impact of Modified Policy on "Me-Too" Drugs with Exogenous Entry

	Change in Levels			Percentage Change		
Change in:	Zoloft	Paxil	Celexa	Zoloft	Paxil	Celexa
effective patent life[a]	-3.58	-2.67	0	-23.9%	-25.6%	0.0%
PV(brand profit)[b]	-2932	-621	-204	-62.8%	-75.2%	-55.8%
PV(generic profit)[b]	-1	-4	-1	-0.2%	-0.9%	-0.5%

[a] Effective patent life is in years.
[b] All dollars are in millions and discounted to January 1991 with a rate of 11%.

Table 2.6: Present Value Welfare Under Exogenous Entry

Change In	Dollars[a]	% Change
Prozac profit[b]	16	0.6%
generic Prozac profit[b]	4042	275.4%
'me-too' brand profit[b]	-3794	-64.0%
'me-too' generic profit[b]	-6	-0.5%
other SSRI profit[b]	-39	-2.4%
other non-SSRI profit[b]	-183	-2.0%
all firms' profit[b]	36	0.1%
insurer savings[c]	10202	-14.4%
consumer welfare[c]	312	1.6%
social welfare	10550	9.4%

[a] Dollars are in millions and discounted to January 1991.
[b] Firms' profits are discounted at 11%.
[c] Insurer savings and consumer welfare are discounted at 5%.

Table 2.7: Distribution Bounds and Average Costs of Phase III Clinical Trials[a]

	Zoloft	Paxil	Celexa
lower bound[b]	1	1	1
upper bound[b]	3198	630	630
mean(cost)[c]	169	170	168
sd(cost)[c]	98	99	98
Prob(entry)[c]	100%	48.5%	88.0%
$I^{PhaseIII}$	–	113	14

[a] All dollar values are in millions.
[b] Lower and upper bounds of the products' respective truncated normal distributions. The upper bounds are calculated as the net present value profit of each product, discounted to the start of Phase III clinical trials, 52 months prior to market entry.
[c] Based on 10,000 random draws for each product.

Table 2.8: Impact of Modified Policy by Molecule[a]

	Change in Levels			Percentage Change		
Change in:	Zoloft	Paxil	Celexa	Zoloft	Paxil	Celexa
effective patent life[a]	-3.58	-2.67	0	-23.9%	-25.6%	0.0%
PV(brand profit)[c]	-2864	-725	-254	-61.3%	-87.8%	-59.0%
PV(generic profit)[c]	35	-237	-18	7.6%	-51.2%	-6.8%

[a] Effective patent life is in years.
[b] Phase III clinical trial costs are weighted by entry decisions and then discounted or inflated to January 1991.
[c] Profits are calculated according to equation (4.11), then weighted by entry decisions and discounted to January 1991. All dollars are in millions.

Table 2.9: Present Value Welfare Under Endogenous Entry

Change In	Dollars[a]	% Change
Prozac profit[b]	16	0.6%
generic Prozac profit[b]	4226	287.8%
'me-too' brand profit[b]	-3844	-64.9%
'me-too' generic profit[b]	-220	-18.5%
other SSRI profit[b]	85	5.2%
other non-SSRI profit[b]	-113	-1.3%
all firms' profit[b]	149	0.6%
saved expenditure[b]	127	
insurer savings[c]	10905	-15.4%
consumer welfare[c]	194	1.0%
social welfare	11375	10.1%

[a] Dollars are in millions and discounted to January 1991.
[b] Firms' profits are discounted at 11%.
[c] Insurer savings and consumer welfare are discounted at 5%.

3

Pharmaceutical Insurance and Generic Entry

3.1 Introduction

We explore how generic-drug availability differentially affects insured and uninsured consumers. Simple logic suggests that generic drugs particularly benefit uninsured consumers. However, we show that this logic might be wrong, because generic prices fall slowly for uninsured consumers, while insurance copayments fall immediately upon generic entry. Being labeled a generic and having a price below the branded drug are sufficient conditions for the insurance copayment to fall, while it is only through competition that the generic price falls. Hence, at least initially, generic entry disproportionately benefits insured consumers.

An extensive literature documents how drug demand responds to prices and ad-

vertising[1] as well as to insurance.[2] We make three contributions to the literature. First, we show how generic availability differentially affects people based on insurance coverage. Second, we account for drug price competition within class and across classes using data on prices and copayments. Finally, we model why branded prices might increase in the face of generic competition.

First, we show how generic availability differentially affects people based on insurance coverage. Immediately after generic entry, copayments fall by more than 50%, while generics often provide only a small discount during the first year (Figures 3.3 and 3.4).

Second, we account for drug price competition within class and across classes. We have monthly data on prescription and over-the-counter prices, as well as insurance copayments for two classes of drugs for fifteen years (1996-2010). Accounting for insurance copayments is a critical component of our analysis. Health care markets are rather distinct in that the price paid by insured consumers (copayment) is typically much smaller than the price received by the manufacturer. With these price data, we estimate elasticities using a discrete choice model similar to Berry et al. (1995).

Finally, we model why branded prices might rise in response to generic competition. Scherer (1993) described this as the "generic paradox" because it is surprising

[1] See Gemmill et al. (2007) and Baicker and Goldman (2011) for surveys of the literature on drug demand and elasticity. After estimating demand, other studies also estimated the welfare implications of pharmaceutical competition, including Chaudhuri et al. (2006); Granlund (2010); Branstetter et al. (2011); Dutta (2011); Arcidiacono et al. (2013); Bokhari and Fournier (2012); Dubois and Lasio (2013); Taylor (2014). In particular, Arcidiacono et al. (2013) estimate the welfare effects of competition among manufacturers of the same molecule, among manufacturers of different molecules in the same class, and among manufacturers of different molecules in different classes. Our paper is unique in estimating the differential effects of generic availability on prices and welfare, according to insurance status.

[2] Expanding health insurance can affect both the quantity and price of health care. Regarding quantity, both the RAND health insurance experiment (Manning et al., 1987) and the Oregon health insurance experiment (Baicker et al., 2013) show that expanding health insurance increases health care consumption, but does not necessarily improve health outcomes. Regarding price, while insurance makes consumers less sensitive to price (Pauly, 1974), insurers sometimes have negotiating power over manufacturers and can drive down prices (Duggan and Scott Morton, 2010), particularly in drug classes with close substitutes (Ridley, 2014).

that a manufacturer would raise prices when faced with new competition.[3] One explanation for the paradox is that a branded manufacturer's profit-maximizing price path is increasing because of consumer learning about quality (Ching, 2010a) and while generic entry causes prices to fall relative to trend, prices nonetheless increase relative to previous periods (Bhattacharya and Vogt, 2003). Another explanation for the generic paradox is that the mix of consumers changes after patent expiration with some consumers switching to generics (Frank and Salkever, 1997). Because we have patient-level data and a structural model, we can create micro moments for patient types and simulate how the profit-maximizing price rises when generic drugs enter the market.

The rest of the paper proceeds as follows. In the next section, we provide background on the antiulcer market and show how it evolved over time. Section 3.3 then describes the demand model and estimation procedure. We present the supply model in Section 3.4. In Section 3.5, we describe the results and their implications for elasticities and producer marginal costs. Lastly, Section 3.6 concludes.

3.2 Background and Data

We examine the "antiulcer" market, as in several previous economic analyses (Berndt et al., 1995, 2003; Arcidiacono et al., 2013; Ridley, 2014). The antiulcer market consists of drugs that treat ulcers as well as acid reflux ("heartburn"). Approximately 10-20% of people in the United States have reflux (Fedorak et al., 2010), and approximately 1% have gastric ulcers (Kurata and Haile, 1984). The therapeutic class of drugs known as H2 antagonists (H2s) were the first to enter the antiulcer market, and were followed by the proton pump inhibitors (PPIs). H2s work by blocking histamine receptors on acid-secreting cells in the stomach lining to inhibit peptic acid

[3] Caves et al. (1991) estimated a negative relationship, while Grabowski and Vernon (1992) estimated a positive relationship between generic entry and price. For example, Regan (2008) found a 1-2% increase in price associated with generic entry.

production. Working more directly than H2s, PPIs inhibit the proton acid pump in the lining of the stomach.[4]

Antiulcer drugs are generally seen as close substitutes by the scientific community, including the FDA which granted priority review to only the first H2 and the first PPI. However, manufacturers of the later products to enter the market assert that their drugs are superior, or at least different, and thus should not be thought of as me-too drugs. For example, the manufacturer of Zantac (the second H2) claims at least five advantages over the first mover, including lower relapse rates, fewer side effects, and more indications (Berndt et al., 1995). Likewise, the fifth PPI, Nexium, is advertised as the "healing purple pill". The FDA-approved label reads: "Nexium 40mg demonstrates higher healing rates in erosive esophagitis than Prilosec 20mg (the approved dose for this indication)". Hence, while the FDA regards the drugs as close substitutes, the manufacturers of these later entrants claim otherwise. Ultimately, the question is whether doctors and patients consider these drugs to be close substitutes. We use a revealed preference approach to investigate the sensitivity of demand to price differences across the drugs, and the welfare effects of newly-available drugs, including generic versions of existing brand name products.

The first H2s came off patent early in our sample period, while the three most recent PPIs remain on patent at the end. Branded H2s entered from 1977 to 1988 and began facing generic competition in 1994 (see Table 3.1). By 2001, all branded H2s faced generic competition, with cimetidine and ranitidine each having more than thirty generic manufacturers. Branded drugs in the PPI class entered between 1989 and 2009 with generic entry beginning in 2002.

[4] While the antiulcer drugs are indicated for short-term treatment, they can be used considerably longer. For example, Nexium is indicated for treatment of heartburn and other symptoms associated with GERD. Its FDA-approved label says that it is indicated for short-term treatment (4 to 8 weeks) in the healing and relief of symptoms associated with erosive esophagitis. However, the label also says that Nexium may be used for additional weeks if the patient has not yet been healed and that the use of Nexium may be continued to maintain the healing.

To capture this market in our analysis, we primarily rely on three data sets. The first is the MarketScan data, which provide a sample of patient-prescription level purchases provided by large employers. Ranging over the period 1996 to 2009, this data allows us to track patient purchases over time.

The second data set was purchased from SDI Health (later acquired by IMS Health) and it provides sales and advertising. The sales data is comprised of monthly prescription drug sales from U.S. retail pharmacies between October 1993 and December 2010. This data include units (for example, number of pills), prescriptions, dollar value, and whether the purchase was done through an insurance plan or paid for out-of-pocket. An important limitation of this data is that the breakout by payment type only starts with January 1996. The advertising data include expenditures targeted at physicians, often referred to as detailing, at the molecule-manufacturer-month level.

Finally, we use information on copayments (the prices consumers face) provide by AdvancePCS, a pharaceutical benefit plan administrator. For a subset of years, the data include copayment by molecule-insurer-month for a subset of the years. The copayment data and details of the insurance market are described below.

3.2.1 Prescriptions

In our analysis, we use retail prescription sales adjusted to daily doses.[5] Figure 3.1 illustrates the evolution of the market's composition by molecule and brand/generic (B/G) status, and shows the relative consumption by molecule. Here, prescriptions are aggregated across all generic manufacturers of the same molecule. Prior to 1993,

[5] The market we examine is restricted along two dimensions. First, we focus on retail sales rather than hospital sales. From 2003 to 2010, retail sales accounted for 91% of PPI prescriptions. We were able to compare retail to hospital sales using another data set with less periodicity (annual rather than monthly) and a shorter time period (2003-2010 rather than 1991-2010). Second, we focus on prescription medications rather than the over-the-counter market. According to an analyst report, over-the-counter drugs accounted for 16% of the retail PPI market from February 2009 to February 2012. Section 3.3.4 describes how we account for over-the-counter availability in our estimation.

H2s controlled the market, with branded ranitidine (Zantac) as the market leader, accounting for over half of all prescriptions. In the mid 1990s, branded omeprazole (Prilosec, the first PPI) became the market leader. Later, branded lansoprazole (Prevacid, the second PPI) became the market leader. In the last five years of the sample, omeprazole (now available as a generic) had a quarter of the market, as did esomeprazole (available exclusively as the branded drug Nexium), with the remaining half of the market distributed across various H2s and PPIs.

Figure 3.1 illustrates the quick growth in the PPI market. The PPI market grew rapidly in part by stealing from the H2 market as can be seen in the decline of the H2 market. However, the total prescription anti-ulcer market was clearly expanding. New entrants to the PPI market advertised heavily. Also, new patients might have entered the market, for instance to seek relief from ulcers caused by non-steroidal inflammatory drugs. Finally, generic entry increased access by dramatically reducing prices (Figures 3.3 and 3.4). With lower generic prices, branded share eroded rapidly. For example, six months after the entry of generic ranitidine, the branded share had fallen by 90%. The impact was similar for the remaining H2s and the PPIs with generic versions. Nonetheless, branded drugs maintain a small segment of the market for a few years after initial generic entry.

The overall evolution of market shares is different for PPIs and H2s, reflecting differences in both business stealing and market expansion. H2 prescriptions peaked in 1995 at just over 3.5 million, but declined steadily thereafter as more PPIs were brought to market. However, combined prescriptions for H2s and PPIs rose dramatically, from just over 2.25 million in 1991 to 9 million by 2011.

Preferences for particular forms may also be important, as the side effects and release times can vary between tablets and capsules.[6] Nizatidine and famotidine have

[6] Breitkreutz and Boos (2011) note that oral forms (i.e. tablets and capsules) are generally preferred, but some patients might not find them easy to swallow, and also note that different

similar branded shares in the 1990s, but dissimilar generic shares in the 2000s. The difference occurs when PPIs are becoming bigger players. A possible explanation for generic famotidine outpacing generic nizatidine is that PPIs are generally of the same form (capsule) as nizatidine and are therefore better substitutes.

3.2.2 Insurance

Insurance complicates the standard demand and supply framework. Insured consumers typically pay a fraction of the total retail prices, while the insurers pay the rest. This reduces the price sensitivity of these consumers and expands the market. However, not all consumers are insured. As shown in Figure 3.2, the proportion of the U.S. population that was uninsured during the years 1996 to 2009 fluctuated between 13% and 16%. This can then be compared to prescriptions sales purchased with cash. These purchases appear fairly stable between 1996 and 2003. Cash purchases fall after 2003 due to at least two factors. First, in 2003 the first over-the-counter PPI is introduced. Cash payers might switch from prescription to over-the-counter. Second, beginning in 2006 Medicare beneficiaries have the option of drug coverage under Medicare Part D, so fewer must pay cash.

3.2.3 Prices

Our price data include the average price per prescription (revenue divided by prescriptions), the wholesale acquisition cost (a list price), and the copay. We have only retail sales data, but retail accounts for 90% of the market for antiulcer drugs. All prices are adjusted to January 2010 dollars.

Figures 3.3 and 3.4 illustrate prices (solid lines) and copayments (dashed lines) for

patients can have different sensitivities to inactive ingredients (which can vary across forms). Jones and Francis (2000) find that, when comparing tablets to capsules, the relative ease of swallowing, perceived speeds of action, and perceived durations of action can all vary from patient-to-patient. As the authors conclude, "consumers have preferences for particular dosage forms."

brands (purple) and generics (green) in the H2 and PPI classes.[7] Typically, branded prices are flat or increasing while generic prices are falling over time. For example, the price of branded cimetidine was approximately $100 in 1994, while generics entered with a price near $75. Over time, the branded price climbed to nearly $150, while the generic price fell below $20. The decline in generic prices might be explained by an increase in generic competition over time, or by falling marginal costs due to learning-by-doing in production. The fact that branded prices do not fall (and often rise) despite the collapse of their market shares suggests the relevant competitive adjustment occurs along a different dimension. From Figure 3.1, however, the fall in H2 generic prices does not appear to be associated with increased prescriptions. This suggests the rise of PPIs — in addition to expanding the prescription market — results in fewer generic prescriptions.

Insured consumers realize the benefit of generic entry through an immediate and often significant reduction of their copays through their insurance plans. The formularies used by these plans generally list a predetermined copay amount that applies to all generic prescription products. Hence, the cost to insured consumers is independent of any competitive behavior beyond generic entry. Figures 3.3 and 3.4 depict these copay prices as dotted lines. The generic copay is significantly lower than the corresponding brand price. For example, it takes 33 months after omeprazole's patent expires for the retail value to match a proportional drop in price observed in the copay value with generic substitution (Figure 3.4a).

In contrast, uninsured consumers benefit little initially from generic entry, because at the outset the generic price is close to the branded price (while the generic copay is half the branded copay). Only after months or years do competitive forces cause a decrease in generic price. Hence, the initial benefit from lower prices for unin-

[7] In Figure 3.3a, the branded price and copay end in 2007, because the branded manufacturer (though not the generic) exits. In Figure 3.3b, the branded price ends because it is truncated at $180 and we want to maintain the same scale across figures.

sured consumers is modest, but grows over time. For example, Figure 3.4a illustrates the prices for both branded and generic 20 mg omeprazole over time. The patent for omeprazole expired in October 2002. The following month, the first generic producer entered the market and immediately began to offer a retail price below the brand producer (solid lines). Two other generic producers entered the market six months later and another three months after that, further competing down the price. The count of generic producers increased to five by 2005 and to eight by 2009. As shown in Figure 3.4a, the average generic retail price continued to decrease throughout this period.

3.3 Demand

3.3.1 Theory

We use a discrete choice model similar to one developed by Berry et al. (1995) to estimate demand in the pharmaceutical market. We start by defining the conditional indirect utility that consumer i obtains from product j, $u_{ij}(\theta)$, as a function of product and consumer characteristics, both observed and unobserved, as well as model parameters θ. The utility function is written as

$$u_{ij}(\theta) = \delta_j(\theta_1) + \mu_{ij}(\theta_2) + \varepsilon_{ij}, \tag{3.1}$$

where $\delta_j(\theta_1)$ is a product-specific term common to all consumers, $\mu_{ij}(\theta_2)$ captures consumer taste heterogeneity for observed product characteristics, and ε_{ij} is the error term, which is assumed to be i.i.d. across both products and consumers. We assume consumer i chooses the product j that yields the greatest utility. Aggregating over all consumer choices then allows us to obtain market shares.

The first component from this equation, $\delta_j(\theta_1)$, is common to all consumers and given by

$$\delta_j(\theta_1) = X_j\beta + \xi_j, \tag{3.2}$$

where X_j is a vector of observed product characteristics, β is a vector of mean taste parameters associated with those characteristics, and ξ_j represents the unobserved (by the econometrician) product utilities.

The second term in the above utility function captures the variation in utility by consumer types across observed characteristics and is given by

$$\mu_{ij}(\theta_2) = \alpha_i p_j + \sum_{\nu} \sum_{k} \gamma_{\nu k} I(i \in \nu) x_{jk}. \tag{3.3}$$

Given that pharmaceuticals are relatively cheap products, we assume away any income effects and interpret α_i to be consumer i's dis-utility of price. The kth characteristic of product j is given by x_{jk} and consumer i is part of a consumer segment, indexed by ν and identified by $I(i \in \nu)$, that have common tastes for the observed characteristics.[8] Let τ_ν denote the probability that consumer i is a type ν. We assume that consumers know their respective types, but the econometrician does not. These terms are then interacted with $\gamma_{\nu k}$, a parameter measuring the heterogeneity across consumer types in tastes for the observed characteristics in the population.

3.3.2 Prices and Copayments

The pharmaceutical industry differs from nearly all other industries in that the patient often pays only a small fraction of the cost of the drug, or copay, while the insurance companies pay the rest.[9] One of the dimensions in which insurance companies compete is through the copay amounts that they set for the drugs available on the market. Hence, we first use the MarketScan data to estimate the relationship between the prices charged by the firms, p_j, and the copay paid by the patient, p_j^c, in the form

$$\ln(p_j^c) = \alpha^c \ln(p_j) + X_j \beta^c + \varepsilon_j^c, \tag{3.4}$$

[8] This approach differs from that in Berry et al. (1995), which allows for consumer-level heterogeneity rather than restricting it to a consumer group level.

[9] The doctor prescribing the drug and the patient together are assumed to be the consumer.

where ε_j^c is i.i.d. across products. Next, we calculate the market-level variance-covariance matrix of drug copays, V^c, from insurance company listings for each drug over time. Taking draws from a standard normal distribution the Cholesky decomposition of V^c then allows us to adjust consumers' price, p_j^c, to reflect consumer types. We can thus capture the fact that consumers in a given insurance plan face a particular menu of prices. In our setting, the random coefficient on price captures this particular form of heterogeneity across consumers. Note that the shape of this heterogeneity is directly informed by the auxiliary dataset on insurance plans.

We restate the utility specification to reflect the substitution patterns among pharmaceutical drugs. Consumer i chooses the drug j that maximizes

$$u_{ij} = \alpha\phi_i(p_j^c) + X_j\beta + \sum_{\nu}\sum_{k}\gamma_{\nu k}I(i \in \nu)x_{jk} + \xi_j + \varepsilon_{ij}, \tag{3.5}$$

where $\phi_i(\cdot)$ is the linear function that adjusts consumers' prices with draws from the Cholesky decomposition of V^c.

3.3.3 Estimation

Based on the approach of Berry et al. (1995), our estimation strategy follows the approach taken by Petrin (2002), who combined both macro (aggregate) and micro (individual) moments to better pin down consumer heterogeneity.

Micro Moments

The MarketScan data are used to generate micro moments (averages) that improve the demand estimation. The GMM estimation routine works by adjusting the parameter estimates so that the average model predictions will match the observed averages from the MarketScan data. In this way, the estimation is improved with the number of distinct micro-moments that are included (Petrin, 2002).

We use a set of three moments to capture the persistence of consumer purchases

over time. Let $d_t = 1$ denote a consumer i's purchase at time t. The first set focuses on the persistence of purchasing any products on the market and are given by

$$\begin{aligned} E[d_{t+1} = 1 | d_t = 1] &= Pr(d_{t+1} = 1 | d_t = 1) \\ E[d_{t+2} = 1 | d_t = 1] &= Pr(d_{t+2} = 1 | d_t = 1) \\ E[d_{t+1} = 1, d_{t+2} = 1 | d_t = 1] &= Pr(d_{t+1} = 1, d_{t+2} = 1 | d_t = 1). \end{aligned} \tag{3.6}$$

The remaining sets center on the persistence of purchasing products with characteristic k. Now let $d_t^k = 1$ denote a consumer i's purchase at time t. The second set of moments are given by

$$\begin{aligned} E[d_{t+1}^k = 1 | d_t^k = 1] &= Pr(d_{t+1}^k = 1 | d_t^k = 1) \\ E[d_{t+1} = 1, d_{t+2}^k = 1 | d_t^k = 1] &= Pr(d_{t+1} = 1, d_{t+2}^k = 1 | d_t^k = 1) \\ E[d_{t+1}^k = 1, d_{t+2}^k = 1 | d_t^k = 1] &= Pr(d_{t+1}^k = 1, d_{t+2}^k = 1 | d_t^k = 1). \end{aligned} \tag{3.7}$$

The specific details for constructing these moments are provided in Appendix B.

Macro Moments

As discussed in Petrin (2002), the underlying approach in Berry et al. (1995) provides two sets of aggregate moments. The first set of moments matches the shares in the data, s_j, to those predicted by the model, $s_j(\delta(\theta), \theta)$, and is given by

$$s_j(\delta(\theta), \theta) - s_j = 0 \quad \text{for } j = 0, 1, ..., J. \tag{3.8}$$

Berry (1994) shows that this equivalence exists and is unique under mild regularity conditions on the distribution of consumer tastes.

The second set of moments relates to market-level unobserved variation, $\xi_j(\theta)$. We assume that this unobserved demand variation for any product is uncorrelated with observed demand-side variables, with the exception of price. This means that

$$E[\xi_j(\theta_0) | X] = 0. \tag{3.9}$$

Instruments for price are derived from the standard sources, as established by Berry (1994).

The Objective Function

Both the macro moments, $G_1(\theta)$, and micro moments, $G_2(\theta)$, feed into the GMM objective function. At θ_0, these moment conditions are assumed to be uniquely equal to zero, i.e.

$$E[G(\theta_0)] = E\begin{bmatrix} G_1(\theta_0) \\ G_2(\theta_0) \end{bmatrix} = 0. \tag{3.10}$$

Hansen (1982) shows that the optimal (two-step) GMM estimator takes the form

$$\hat{\theta} = \arg\min_{\theta \in \Theta} G^*(\theta)' G^*(\theta), \tag{3.11}$$

where $G^*(\theta) = a(\tilde{\theta})\hat{G}(\theta)$, $\hat{G}(\theta)$ is the sample analogue of $G(\cdot)$, and $a(\tilde{\theta})$ is a consistent estimate of the "square root" of the inverse of the asymptotic variance-covariance matrix of the moments (obtained using $\tilde{\theta}$, a preliminary consistent estimate of θ_0).

3.3.4 Market Size and the Outside Good

To form our sample, we start by following the established path of defining daily dose as a common basis of comparison to allow for estimation of substitutability between products (Stern, 1996a; Berndt et al., 1997). These values are then scaled up to the monthly level to correspond to the common duration of prescriptions. To construct the size of the market and the share of the outside good, we assume the market for H2 antagonists and PPIs is 20% of the total U.S. population, which is in the range reported by Fedorak et al. (2010). Multiplying the U.S. population by the 20% prevalence gives the market size.

The market for antiulcer drugs also includes over-the-counter products that are available without prescription. While this part of the market for H2s and PPIs

represents a small share of the market, it is still an important factor to consider.[10] We account for changes in the over-the-counter market in two ways. First, we include a dummy variable for whether a given molecule is also available in over-the-counter form and interact this variable with generic status. This dummy enables us to include competitive effects of the over-the-counter products to vary by brand/generic status as well as to allow us to relax the assumption that when a PPI goes over-the-market it affects all PPIs in the same way. Second, we include time dummies that are interacted with the therapeutic drug class. This means that the over-the-counter drugs can differentially affect each class, even though the effect on products within each class may be more similar. Together, these steps allow us to more flexibly account for the effects of over-the-counter products.

In estimating the demand, we consider both time-varying and time-invariant effects. We allow for time-varying product characteristics, X_{jt}, to enter the consumer's utility (any time-invariant characteristics will be subsumed by the product-specific fixed effects). First, as described above, we allow for time dummies that vary by class. This is important because consumer perceptions and over-the-counter offerings may change over time. Additionally, we incorporate time-since-entry dummy variables for each of the first twelve months after product entry, which may capture product availability or aspects of consumer awareness. These dummies are allowed to vary by therapeutic class. We also include cumulative log advertising at the molecule-manufacturer-month level.[11] As discussed in the data section, our measure of advertising is detailing, which only occurs for branded products. All variants of the same molecule are assumed to receive the same utility gain from advertising.

[10] According to an analyst report, over-the-counter drugs accounted for a mean of 16% (standard deviation of 2%) of the retail PPI market from 2009 through 2011 (BofA Merrill Lynch Global Research using IMS Health prescription data and Nielsen over-the-counter data, April 2012).

[11] In previous studies of the effect of detailing on demand for antiulcer drugs, the estimated depreciation rate for the (detailing) advertising stock was zero percent (Berndt et al., 1995; Ling et al., 2002; Ridley, 2014). Hence, we use the advertising stock with zero depreciation.

This paper treats advertising as exogenous. Pharmaceutical manufacturers typically lay out their advertising schedules far in advance and these schedules do not appear sensitive to monthly demand shocks that are commonly absorbed by the error term. Finally, we include product-level fixed effects, where a product is defined at the manufacturer-molecule-form level.

Identification

We use a panel of consumer-level data to generate average persistence of purchase behavior across a number of product characteristics. This extra information allows us to better estimate substitution patterns to reflect differences in taste for product characteristics that are driven by demographics. In particular, by matching persistence in choice, as it relates to observed product and consumer characteristics, we are able to pin down individual heterogeneity parameters. Our choice of micro moments is driven by the parameters we are seeking to identify.

3.4 Supply

In order to perform policy simulations, we need to impose a supply side model. This then allows us to determine how producers react when uninsured consumers become insured. Following the empirical industrial organization convention, we assume a unique static, multi-product Bertrand Nash equilibrium in prices.

For each firm f at time t, let $\mathcal{J}_f$ index the firm's portfolio of products. The profits of firm f are then given by

$$\Pi_f = \sum_{j \in \mathcal{J}_f} (p_j - mc_j) M s_j(p) - a_j - C_f, \tag{3.12}$$

where $s(p)$ is the market share of product j, mc_j is its marginal cost, M is the size of the market, a_j is the cost of advertising, and C_f is the fixed cost of production.

Under our equilibrium assumption, the price, p_j, and the implied marginal cost, $\widehat{mc}_j$, must then satisfy the following first-order condition (FOC):

$$s_j(p) + \sum_{r \in \mathcal{J}_f} (p_r - \widehat{mc}_r) \frac{\partial s_r(p)}{\partial p_j} = 0. \tag{3.13}$$

The J_f equations in (3.13) can be used to calculate the price-cost margins for each product. We define

$$\Omega_{jr}(p) = \begin{cases} -\partial s_r(p)/\partial p_{jt} & \text{if } \exists f : r, j \in \mathcal{J}_f \\ 0 & \text{otherwise} \end{cases} \tag{3.14}$$

and substitute it into the vector form of the FOC to get

$$s(p) - \Omega(p)(p - \widehat{mc}) = 0. \tag{3.15}$$

Assuming $\Omega(p)$ is non-singular, this equation can then be rearranged and used to solve for the markups and implied marginal costs:

$$p - \widehat{mc} = \Omega(p)^{-1} s(p) \quad \text{and} \quad \widehat{mc} = p - \Omega(p)^{-1} s(p). \tag{3.16}$$

In addtion to providing marginal costs if they are not observed, this equation can be used to simulate the equilibrium prices in our policy experiments.

3.5 Results

We start with the copay-price relationship defined in equation 3.4, the results of which are presented in Table 3.2. As expected, we see a positive relationship between copay and price; that is, more expensive drugs are assigned higher copays. Taking into account the adjustments outline in Section 3.3.2, these parameters are used to form copayments for the entire sample period.

The non-linear parameters, which capture the consumer types, are presented in Table 3.3. Normalizing against the coefficients of consumers of type 1, we estimate

for each of the other four consumer types the coefficients on dummies for having any purchase (Buy), and purchasing a PPI (PPI), brand (Brand), and tablet formulation (TAB). We also interact these dummies with an index of time (Time), which is scaled down by 100. Finally, we report the probability of a consumer being each of the specified types. These results indicate that most consumers are of type 3, who do not buy often, but have a strong preference for generic PPIs in capsule form. The second most prevalent group is consumers of type 5 and they buy a little more often than consumers of type 3, but have a preference for branded PPIs. Consumers of type 2 are similar to those of type 3, except they have a preference for the tablet form that increases with time. Most of the estimates are significant, which validates the approach of distinguishing between discrete consumer types.

Table 3.4 presents the results of selected linear parameters. As we would expect, the price and advertising coefficients imply that consumers prefer products that are lower priced and those that are advertised heavily, all else equal. For PPIs, advertising has less of an impact, which may be due to consumers' high awareness of the availability of antiulcer drugs from the advertising on H2 products. This is consistent with the results found in Arcidiacono et al. (2013). Interestingly, the time-since-entry coefficients show no noticable trend in consumer purchases in the first 12 months.

3.5.1 Elasticities

We present the elasticities for own and cross-price effects in Tables 3.5 and 3.6 for December 2005 and 2010, respectively. In these tables, price changes along each row affect the market shares of the products in each column. We report the weighted average elasticities across sales to insured and uninsured consumers for all branded drugs as well as for the most popular generic version of each molecule. As expected, uninsured consumers are consistently more price sensitive then their insured coun-

terparts. This difference has important implications for the impact of extending insurance to those consumers that are currently uninsured. Additionally, all own-price elasticities are negative and greater than one in magnitude, which is consistent with the economic theory. The cross-price effects are larger for products that have larger market shares. However, given the form of our model, the effects from a price change of a given product are mostly independent of the characteristics of any other product. Notably, the PPIs are closest substitutes to other PPIs, as one might expect. On the other hand, H2s are more likely to lose share to a PPI, as opposed to another H2.

3.5.2 Marginal Costs

Once we have our demand estimates, we can use the supply-side model and assumptions to calculate the implied marginal costs. In Figure 3.5, we present these results for the two most recent products to experience generic entry within our sample period. The vertical dashed lines indicate the timing of the initial generic entry. Interestingly, there is little to no response to generic entry on both lansoprazole and pantoprazole. These findings deviate from much of the prior literature that uses models with a logit error.

3.6 Conclusion

Using data from the pharmaceutical industry, we estimate demand and supply for prescription drugs across both insured and uninsured consumers, allowing for consumer preferences organized into discrete types. We account for an important characteristic of health care markets: the price paid by insured consumers (copayment) is typically much smaller than the price received by the manufacturer. Our analysis highlights how generic-drug availability differentially affects insured and uninsured consumers. In particular, generic entry disproportionately benefits insured

consumers, at least in the first year to two years.

The estimates from our models of demand and supply allow for the examination of policy experiments. Among the potential experiments is examining the welfare impact of the insurance expansion under the Affordable Care Act (ACA or "Obamacare"), as it impacts consumers, producers, and insurers. Insurance expansion creates possible spillovers for manufacturers. In ongoing work, we will estimate the increase in profit, isolating the price effect from the quantity effect. Additionally, we will do a back-of-the-envelope calculation in which we compare the profit increase associated with the ACA to the tax imposed on manufacturers to help pay for the insurance expansion. Congress anticipated the profit windfall pharmaceutical manufacturers would gain from the expansion of insurance under the ACA and created a tax on pharmaceuticals (to help pay for the insurance expansion). Section 9008 of the Affordable Care Act set forth the Branded Prescription Drug Fee Program. The government sums sales to the government (Medicare, Medicaid, military, veterans) and then taxes manufacturers on this basis.[12] The ten-year cost to manufacturers is expected to be $30 billion.[13]

[12] http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Branded-Prescription-Drug.html

[13] http://www.forbes.com/sites/brucejapsen/2013/05/25/obamacare-will-bring-drug-industry-35-billion-in-profits/

Table 3.1: Market Entry by Molecule

Class	Molecule	Brand Name	Brand Entry	OTC Entry	1st Gen Entry	Gen Entrants	List of Forms†
H2	cimetidine	Tagamet	Aug-77	Aug-95	May-94	36	Tab
	ranitidine	Zantac	Jul-83	Apr-96	Jul-97	32	Tab, Cap
	famotidine	Pepcid	Nov-86	Jun-95	Apr-01	19	Tab
	nizatidine	Axid	May-88	Jul-96	Jul-02	9	Cap
PPI	omeprazole	Prilosec	Oct-89	Sep-03	Nov-02	12	Cap
	lansoprazole	Prevacid	May-95	Nov-09	Nov-09	4	Cap, Tab
	rabeprazole	Aciphex	Sep-99	-	-	-	Tab
	pantoprazole	Protonix	Apr-00	-	Dec-07	4	Tab
	esomeprazole	Nexium	Feb-01	-	-	-	Cap
	omeprazole $NaHCO_3$	Zegerid	Oct-04	Mar-10	Jul-10	2	Cap
	dexlansoprazole	Dexilant	Feb-09	-	-	-	Cap

† Forms are listed in order of popularity.

Table 3.2: Regression results. Dependent variable is Ln(copayment)

	Coefficient	Standard Error
Constant	2.558	(0.279)
Ln(price)	0.113	(0.056)

N=100. Observations are at the insurance group-molecule-month level.

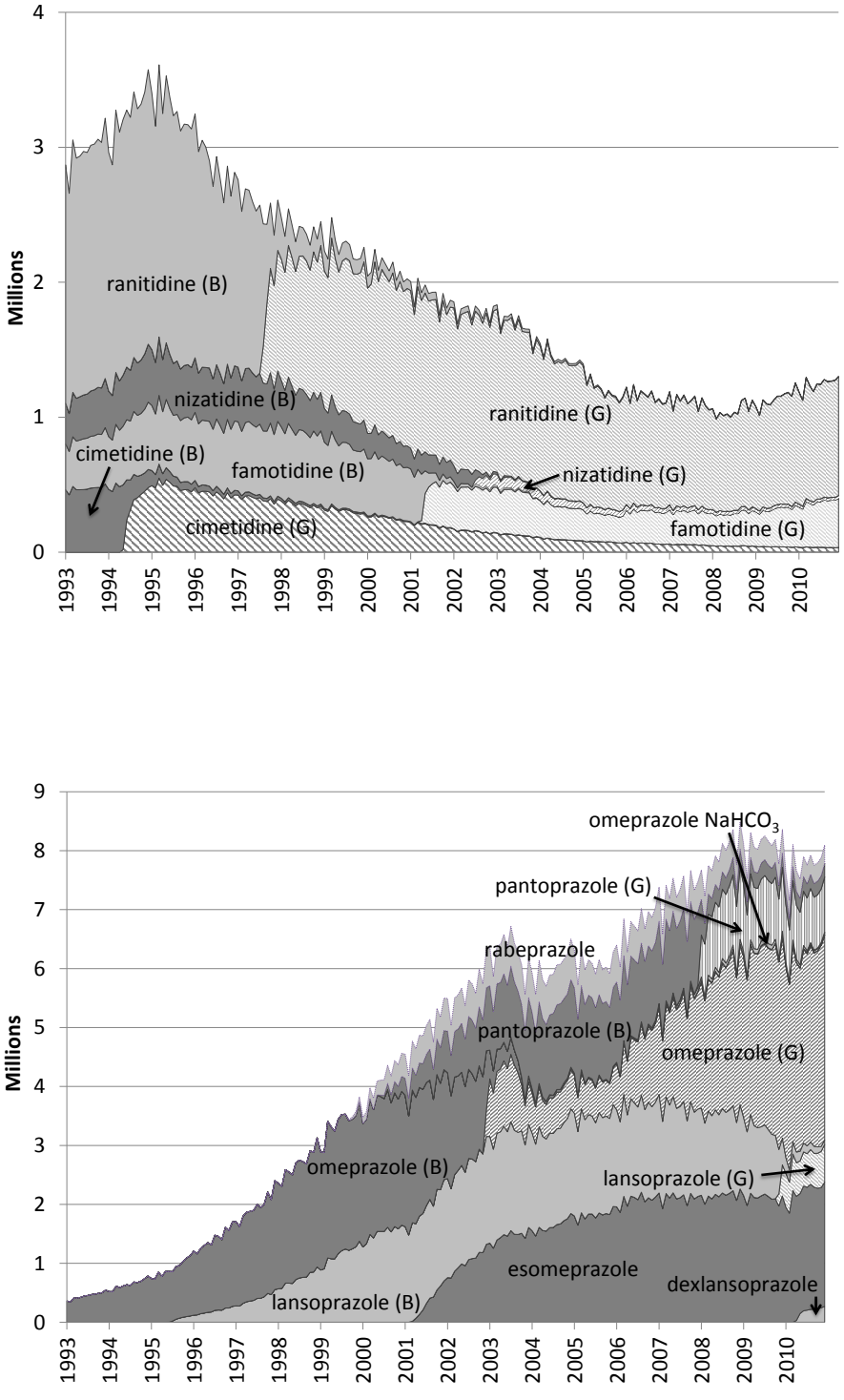


FIGURE 3.1: Monthly Prescriptions for H2 and PPIs.

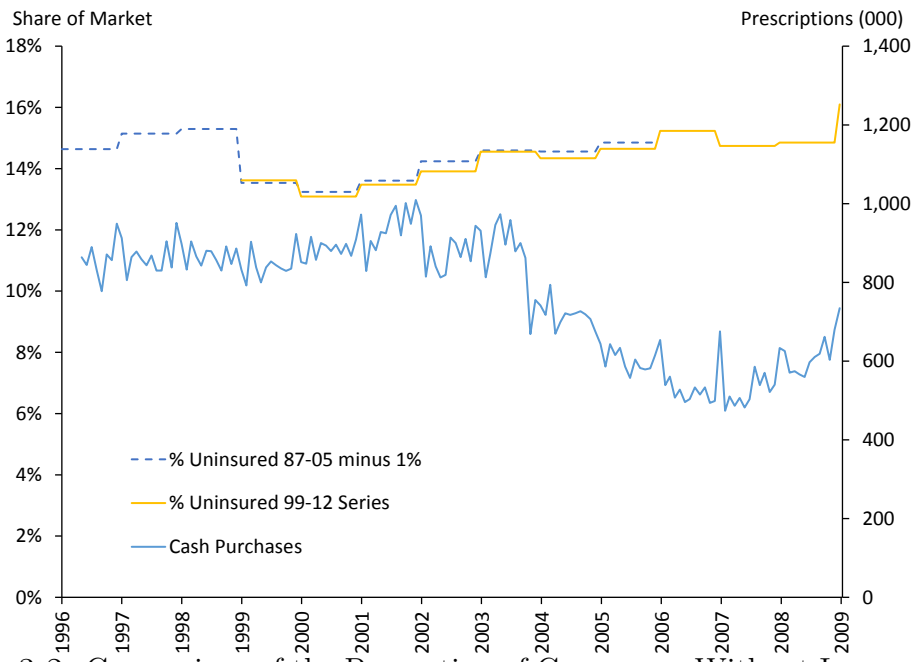
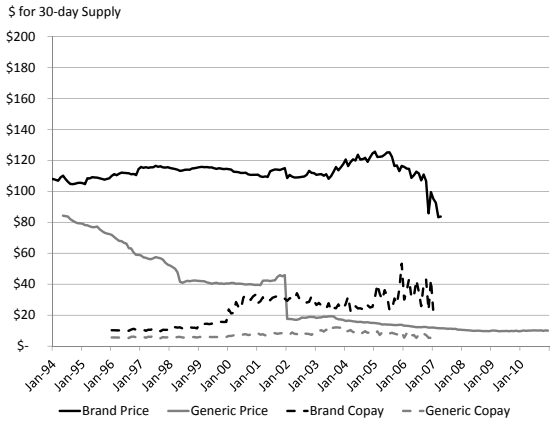
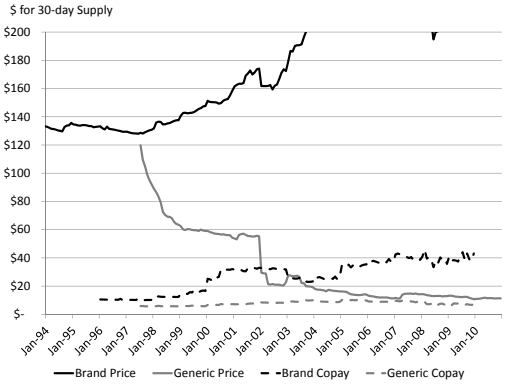


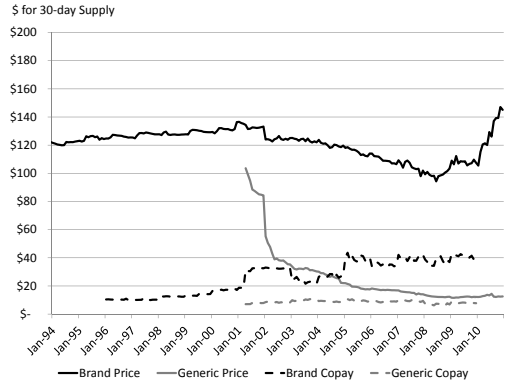
FIGURE 3.2: Comparison of the Proportion of Consumers Without Insurance to the Proportion Prescriptions for H2s and PPIs Purchased by the Uninsured.



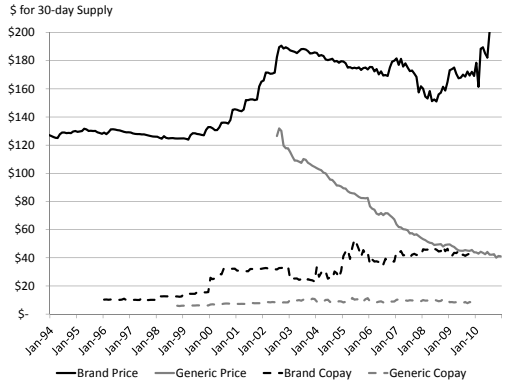
(a) cimetidine



(b) ranitidine

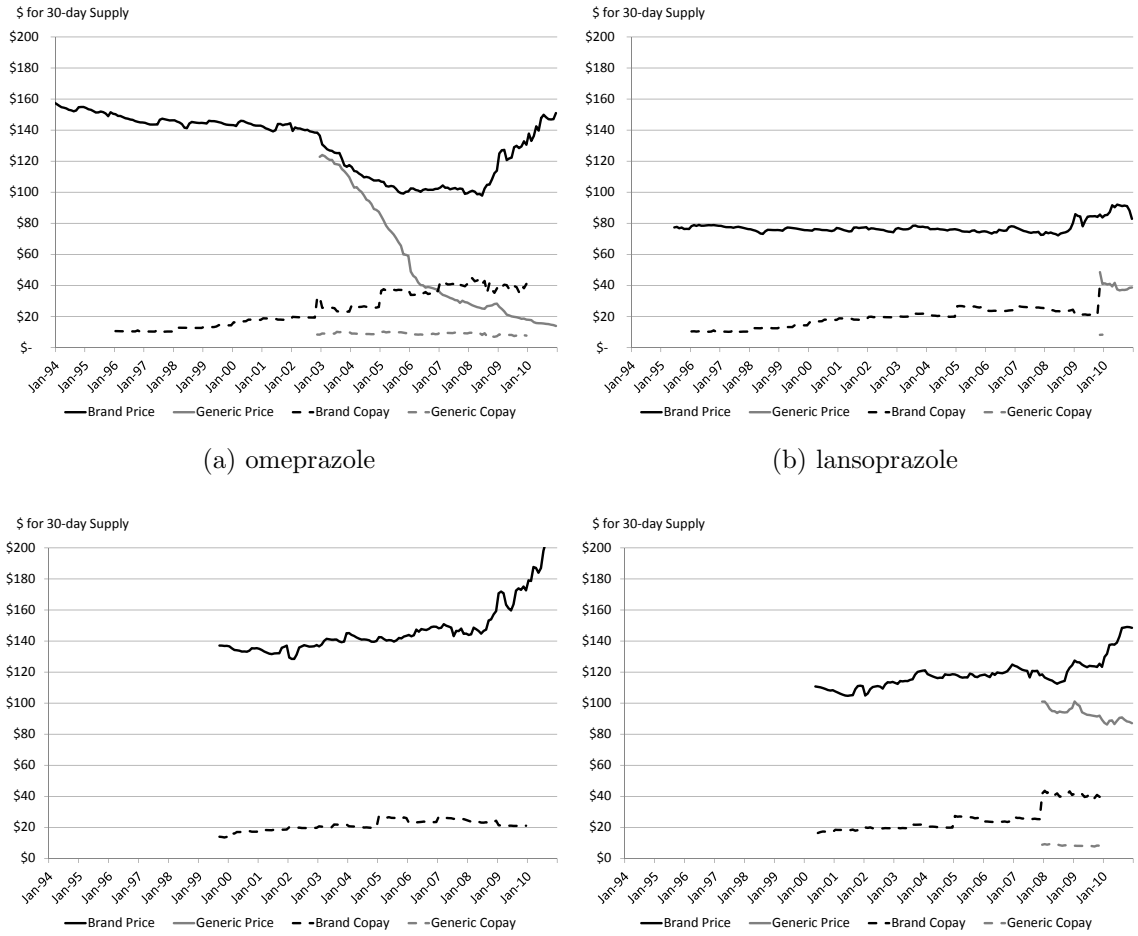


(c) famotidine



(d) nizatidine

FIGURE 3.3: Retail Prices and Copayments for Branded and Generic H2 Drugs.



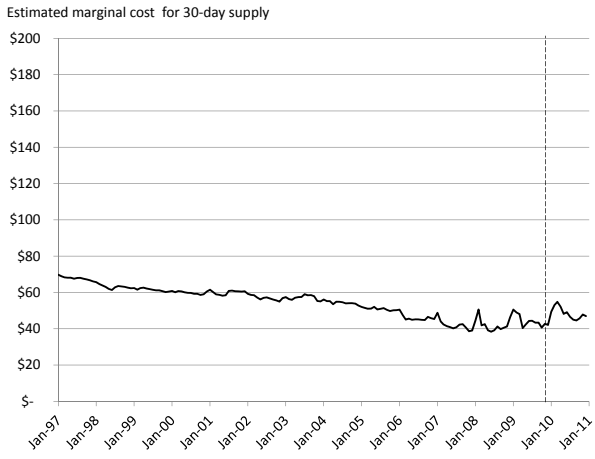
(a) omeprazole

(b) lansoprazole

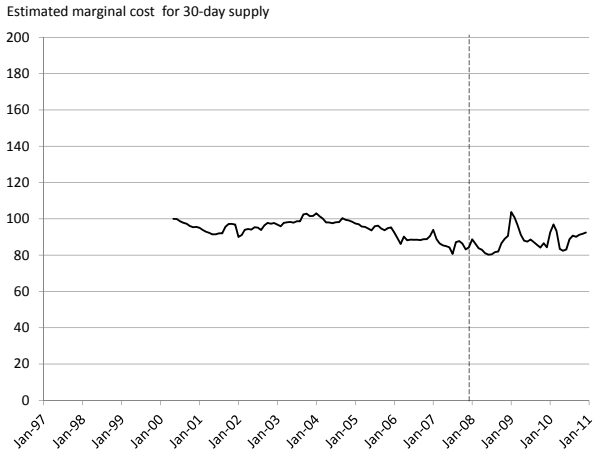
(c) rabeprazole

(d) pantoprazole

FIGURE 3.4: Retail Prices and Copayments for Branded and Generic PPI Drugs.



(a) lansoprazole



(b) pantoprazole

FIGURE 3.5: Marginal Costs for Selected Molecules.

Table 3.3: Non-Linear Parameters

	Type 2		Type 3		Type 4		Type 5	
	Coefficient	Standard Errosr	Coefficient	Standard Errors	Coefficient	Standard Errors	Coefficient	Standard Errors
Buy	-2.2000	(0.0159)	-2.9658	(0.8979)	0.9579	(0.3046)	-1.1072	(0.0236)
Buy*Time	-4.1137	(0.0148)	-2.6042	(1.5666)	-0.6085	(0.0732)	-1.5325	(0.0200)
PPI	0.0911	(0.0068)	0.7903	(0.0595)	0.2143	(0.0002)	2.1526	(1.2747)
PPI*Time	1.0443	(0.0086)	1.9990	(0.6097)	0.2074	(0.0007)	-0.6051	(0.0625)
Brand	-0.5679	(0.0189)	-0.2118	(0.8652)	-2.0265	(0.0493)	0.9524	(0.4427)
Brand*Time	-0.1160	(0.0169)	-0.3148	(1.6976)	-1.9010	(0.0450)	-0.1566	(0.1445)
TAB	-0.0170	(0.0311)	-2.5700	(0.2898)	-1.5156	(0.1212)	-3.6673	(0.2469)
TAB*Time	0.9945	(0.0052)	4.8079	(0.0057)	3.8878	(1.1398)	6.4004	(0.1902)
Pr(type)	0.0873	(0.0046)	0.7245	(0.0305)	0.0413	(0.0001)	0.1120	(0.0002)

N=15749. Parameter estimeates are normalized to consumers of Type 1.

Table 3.4: Linear Parameters

			Interaction with PPI	
	Coefficient	Standard Errors	Coefficient	Standard Errors
Copay	-0.5179	(0.1431)		
Own-Molecule OTC	-0.9037	(3.0866)		
Brand x Own-Molecule OTC	-7.6415	(3.0205)		
Insured	-27.3797	(7.8701)		
Insured x Generic	12.9805	(3.5871)		
Brand x generic competition	-2.3346	(1.1860)	-5.3412	(3.6789)
Ln Cumulative Advertising	15.7669	(6.4262)	-10.5903	(5.6963)
1 month on market	0.2394	(1.4018)	1.2539	(2.347)
2 month	1.7433	(1.4945)	1.5980	(2.2507)
3 month	1.2599	(1.3156)	3.0780	(2.3119)
4 month	1.2433	(1.2819)	3.5177	(2.4054)
5 month	1.4406	(1.2818)	3.1143	(2.3962)
6 month	1.5529	(1.2691)	2.8323	(2.3771)
7 month	1.5754	(1.2529)	3.3596	(2.4690)
8 month	1.5056	(1.2339)	2.9270	(2.4360)
9 month	1.4812	(1.2140)	2.6891	(2.4240)
10 month	1.3663	(1.1925)	2.8399	(2.4399)
11 month	1.2535	(1.1708)	3.3848	(2.5004)
12 month	1.3214	(1.1714)	3.1762	(2.4805)

N=15749. Estimated jointly with non-linear parameters. Also includes manufacturer-molecule-form fixed effects, month dummies, and month dummies cross PPI. There are 600 linear parameters.

Table 3.5: Elasticity and Cross Price Elasticity Estimates for December 2005

			H2 Brand				H2 Generic				PPI Brand						PPI Generic
		Share	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*esomeprazole*	*lanso. (cap)*	*lanso. (tab)*	*omeprazole*	*pantoprazole*	*rabeprazole*	*omeprazole*
H2 B	cimetidine	0.00	-1.3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	famotidine	0.01	0.00	-6.63	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	nizatidine	0.00	0.00	0.00	-6.83	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.03	0.00	0.00	0.00	-7.69	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
H2 G	cimetidine	0.07	0.00	0.00	0.00	0.00	-1.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	famotidine	0.19	0.00	0.00	0.00	0.00	0.00	-1.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	nizatidine	0.03	0.00	0.00	0.00	0.00	0.00	0.00	-3.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.71	0.01	0.01	0.01	0.01	0.01	0.01	0.01	-1.42	0.01	0.01	0.01	0.01	0.01	0.01	0.01
PPI B	esomeprazole	9.80	0.14	0.22	0.19	0.20	0.25	0.22	0.18	0.20	-2.63	0.18	0.20	0.18	0.20	0.18	0.16
	lanso. (cap)	7.75	0.11	0.19	0.16	0.17	0.22	0.19	0.15	0.17	0.15	-3	0.17	0.15	0.17	0.15	0.13
	lanso. (tab)	0.36	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	-3.19	0.01	0.01	0.01	0.01
	omeprazole	0.35	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	-3.47	0.01	0.01	0.01
	pantoprazole	3.30	0.05	0.13	0.1	0.11	0.15	0.12	0.09	0.11	0.08	0.09	0.1	0.08	-5.18	0.09	0.07
	rabeprazole	1.62	0.02	0.06	0.05	0.05	0.06	0.05	0.04	0.05	0.04	0.04	0.05	0.04	0.05	-4.52	0.03
PPI G	omeprazole	0.68	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	-2.05

Rows correspond to price changes and columns correspond to quantity changes. Shares for generics correspond to the top-selling generic of that molecule.

Table 3.6: Elasticity and Cross Price Elasticity Estimates for December 2010

			H2 Brand		H2 Generic				PPI Brand							PPI Generic		
		Share	*famotidine*	*ranitidine*	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*dexlansoprazole*	*esomeprazole*	*lanso. (cap)*	*lanso. (tab)*	*omeprazole*	*pantoprazole*	*rabeprazole*	*lansoprazole*	*omeprazole*	*pantoprazole*
H2 B	famotidine	0.00 %	-1.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.01 %	0.00	-5.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
H2 G	cimetidine	0.12 %	0.00	0.00	-1.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	famotidine	0.65 %	0.01	0.01	0.01	-1.43	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	nizatidine	0.03 %	0.00	0.00	0.00	0.00	-1.93	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.97 %	0.01	0.01	0.01	0.01	0.01	-1.69	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
PPI B	dexlansoprazole	1.54 %	0.02	0.02	0.03	0.02	0.02	0.03	-1.77	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	esomeprazole	12.80 %	0.19	0.20	0.22	0.21	0.20	0.25	0.20	-1.63	0.21	0.20	0.20	0.19	0.20	0.20	0.20	0.20
	lanso. (cap)	0.29 %	0.00	0.01	0.01	0.01	0.01	0.01	0.00	0.00	-3.28	0.01	0.01	0.00	0.00	0.00	0.01	0.00
	lanso. (tab)	0.15 %	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	-3.99	0.00	0.00	0.00	0.00	0.00	0.00
	omeprazole	0.04 %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-5.27	0.00	0.00	0.00	0.00	0.00
	pantoprazole	0.75 %	0.01	0.01	0.02	0.02	0.01	0.02	0.01	0.01	0.01	0.01	0.01	-2.67	0.01	0.01	0.01	0.01
	rabeprazole	1.01 %	0.02	0.02	0.03	0.02	0.02	0.04	0.02	0.02	0.02	0.02	0.02	0.02	-3.28	0.02	0.02	0.02
PPI G	lansoprazole	1.80 %	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.02	0.03	0.03	0.03	0.02	0.03	-1.65	0.03	0.03
	omeprazole	7.84 %	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	-1.09	0.09
	pantoprazole	2.16 %	0.03	0.04	0.05	0.04	0.04	0.06	0.03	0.03	0.04	0.04	0.04	0.03	0.03	0.03	0.04	-2.40

Rows correspond to price changes and columns correspond to quantity changes. Shares for generics correspond to the top-selling generic of that molecule.
Relative to 2005 (Table 3.5), there are fewer branded H2 antagonists and more generic PPIs available in 2010.

4

Patent Breadth versus Length with High-Value Followers

4.1 Introduction

Patent policy maximizes social welfare by promoting the creation of valuable innovations and limiting the costs that stem from market distortions and duplicative spending. The standard levers of these policies are patent breadth, which restricts competitive imitation (the scope of protection), and patent length, which specifies the amount of time the protection can be enforced. The first empirical assessment of the trade-off between these levers is provided in Chapter 2, which uses data from the U.S. pharmaceutical industry to show that under certain conditions social welfare can be improved.[1] In this chapter, I ease one of the main assumptions made in that analysis to allow for a more generalized framework and determine if the results still hold.

In order to make this problem more tractable, Chapter 2 highlights features of the pharmaceutical industry and relies on a number of assumptions. In particular, product innovations in this industry are exogenously categorized based on their target

[1] Chapter 2 corresponds to Taylor (2014).

in the body (mechanism of action). Products in the same category, called therapeutic class, are therefore very similar in their use and benefits. Chapter 2 examines the impact of expanding patent breadth from the chemical composition (molecule) level to the therapeutic class level. To simplify the analysis, that chapter assumes that while the first innovation in a class is a high-value product, all that follow are "me-too" drugs that provide relatively little, if any, added therapeutic value to the market beyond the first. However, this is often not the case. A notably relevant example is Lipitor, which was the sixth innovation to enter the therapeutic class of statins (cholesterol drugs), but is the best-selling drug of all time. The highly successful drug Zoloft provides another example as the second antidepressant to target the serotonin reuptake mechanism in the body. In this chapter, I ask the following question: Do the results from Chapter 2 still hold when an innovation that is not first-in-class is considered to be high-value and provided with the modified patent?

As a simple motivating example, consider a market with two product innovations and suppose both are high value, i.e. the second provides major therapeutic value to consumers beyond the first. Under the assumption in Chapter 2, only the first innovation would receive the modified patent, while the second would be delayed from entering the market. However, this would mean that consumers would suffer a significant loss in this delay, which could potentially last a number of years. Now suppose that the remaining patent life on the second innovation after the delay is too short to allow the innovator to make sufficient profit on its investment in the third phase of clinical trials. In this setting, the innovator would choose to abandon the innovation and retain this investment. In turn, this would mean the permanent loss for consumers of the brand product as well as the generics that would have followed. The net impact of this scenario could result in a large social welfare loss. For this reason, it is important to ease the restriction in Chapter 2 and allow for the potential that later innovations into the market are high value.

I use estimates from the static model of demand presented in Chapter 2 in order to implement the analysis in this chapter. The model allows for the quality of products to be determined by consumer preferences. It is then assumed in the policy experiments which products are high-value innovations and which are "me-too"s. The first policy experiment modifies the patent of all high-value innovations to limit the profit, and therefore the incentives to develop "me-too" drugs. Specifically, I expand the patent breadth and limit the patent length of the high-value antidepressants, Prozac and Zoloft, in order to temporarily restrict the subsequent "me-too" products in the same therapeutic class from entering the market. I find that the patent lives of Prozac and Zoloft are shortened by 26 months and 52 months, respectively. Additionally, the \$1.4 billion in lost profits (49.8%) suffered by "me-too" innovators is overshadowed by the \$8.3 billion in savings (11.3%) realized by insurers. Finally, consumers experience a welfare gain of \$166 million (0.8%) under the modified framework. The total social impact of this modified policy is a gain of more than \$9.1 billion (7.9%).

The second counterfactual builds on the first, by allowing the "me-too" innovators to anticipate the impact of the modified policy on their expected profits and reoptimize their entry decisions during their respective drug development processes. Those innovators that abandoned their drugs save their remaining investment expenditures. I find that while Lexapro would always proceed through Phase III clinical trials and onto the market, Paxil and Celexa would do so with probabilities of only 18.1% and 5.8%, respectively. The net effect on producers is a gain of \$1.1 billion (5.0%) due to the expenditures saved by entry re-optimization. In cases where the products do not enter the market, consumers lose the value of their entry as well as the generics that would have followed on each molecule. Diverging from the results in Chapter 2, this effect is larger than the benefit that consumers gain from earlier generic entry on the molecules for both Prozac (fluoxetine) and Zoloft (sertraline),

and leads to a consumer loss of $84 million (0.4%). However, insurers still realize large gains ($8.3 billion or 11.3%) as consumers who would have otherwise purchased Paxil and Celexa, turn to generic fluoxetine and sertraline instead. The net social welfare effect sums to $9.3 billion (8.1%). These results indicate the potential for meaningful social gains from exploring modified patent policies in a more realistic setting.

While this work extends the study of the tradeoff between patent breadth and length, some aspects of the problem are still not addressed. For example, this chapter does not try to address the question of how much the initial innovators should be rewarded; instead, like most of the theory literature, it considers how to give the initial innovator a fixed reward. Additionally, the analysis includes only a limited range of dynamics. While "me-too" innovators are allowed to reoptimize their entry decisions, the decisions of other market participants are assumed to be exogenous and held fixed. At the end of the chapter, I discuss ongoing work that seeks to address this last limitation.

I proceed in the chapter by first providing some background to highlight important features of the market that are relevant for this analysis.[2] In Section III, I implement the counterfactual simulations to measure the welfare implications on consumers, insurers, and producers (innovators and manufacturers). Finally, Section IV concludes.

4.2 Background

In this section, I provide some brief background information relevant to the market that allow me to implement the policy experiments. A full description of the industry and data are provided in Chapter 2.

[2] Readers should refer to that Chapter 2 for a review of the related literature and a full description of the industry, data, and the model of demand and supply with the corresponding results.

The antidepressant market is dominated by two therapeutic classes. The first class is often referred to as Other Antidepressants or as New Generation Antidepressants (NGAs) and these products appear to allow for increased levels of norepinephrine and dopamine in the brain. On the other hand, the second and more prominent of the two classes consists of selective serotonin reuptake inhibitors (SSRIs), which elevate only serotonin in the brain. Nearly all of the antidepressant products sold under patent between 1991 and 2010 belong to either the SSRIs or NGAs. Table 4.1 provides details on the top selling products in each class, including launch and patent expiration dates.

As shown in Figure 4.1, SSRIs sales were dominated by Prozac and Zoloft. The SSRIs began in 1988 with the market introduction of Prozac, which immediately became the most prevalent product in the market with annual sales of over $1 billion. Following on Prozacs success, Zoloft was released in early 1992 and successfully competed for sales. Paxil entered the market in the beginning of 1993 and Celexa, in the second half of 1998, but neither attained the same success. Finally, Lexapro entered the market in the second half of 2002 and achieved greater success than either Paxil or Celexa, despite its entry into the market after Prozac's patent expired. Zoloft's success during this period may be due to a number of reasons including valuable therapeutic differences, pricing, and marketing. For example, Prozac and Paxil have a higher risk of some drug interactions than does Zoloft (Spina and Scordo, 2002). In the analysis that follows, I treat both Prozac and Zoloft as high-value innovations, while the subsequent entrants are assumed to be "me-too"s.

4.3 Modified Policies

This section provides a framework that measures the welfare implications of modifying patent breadth and length, which is then applied to the pharmaceutical industry. My analysis is informed by features of the market as well as estimates of consumers'

substitution behavior that come from the demand model presented in Chapter 2. As noted above, this model allows for the quality of products to be determined by consumer preferences. In the policy experiments, I then assume that Prozac and Zoloft are high value innovations and the later innovations are "me-too"s.

4.3.1 Overview

The abstract search for an optimal patent policy is limited to what is feasible for a given market. Any analysis that searches for an optimal patent policy requires that the measure of patent breadth be defined in such a way that is known to the market and independent of any decisions made by the firms. For the pharmaceutical industry, there are three such feasible levels for breadth. The narrowest is the molecule level, which is the breadth specified under the existing policy. The other two are the therapeutic class level and the entire market. I expand breadth to the therapeutic class and then scale the patent length in order to make the high-value innovator indifferent between the two policies.[3]

For my policy experiments, I model patent breadth on the high-value innovation as the degree to which it can restrict "me-too" products from entering the market, but not other high-value innovations that may follow.[4] The "me-too" innovators that are restricted from the market retain ownership of their patents under the modified policy.[5] The implication of this is that once the patent on the high-value product expires or a second high-value product enters the market, the "me-too" products

[3] This follows the conceptual framework in much of the prior literature.

[4] As discussed in Section 2.3.1, the temporal disconnect between when an innovation is patented and when its value is known implies that the conventional framework of patent policy is not well suited for examining alternative levels of patent breadth and length.

[5] While I ignore the possibility that a drug may be used for multiple completely different markets (treatments), it is a simple matter to focus the entry restriction to only a specified market and still allow access in other markets. For example, the popular hair treatment Rogaine (minoxidil) is also used to treat high blood pressure (under the trade name Loniten). Even if it had temporarily been blocked as a high blood pressure medication, as the first hair growth drug approved by the FDA, it would be free to enter this second market.

that were delayed by the first high-value product can then enter the market.

For the purpose of exposition, Figure 4.2 depicts the profit over time for multiple high-value innovations, m_0 and m_2, as well as multiple "me-too" innovations, m_1 and m_3. By design, m_2 provides significant added therapeutic value beyond m_0, while m_1 and m_3 are "me-too"s of m_0 and m_2, respectively. Upon their entry, the "me-too" products negatively impact the profit of the high-value products. I propose a policy modification whereby the patent breadth of m_0 is increased so as to delay the market entry of m_1, but not m_2. The entry of m_2 transfers the expanded patent breadth from m_0 to m_2, which allows m_1 to enter the market and delays the entry of m_3. The patent lives of m_0 and m_2 are each limited to ensure at least the same net present discounted profit earned under patent protection, V^f. This means that the delay of m_2's entry onto the market also affects the patent length of m_0. Figure 4.3 illustrates the shift in the timing of market entry for each market participant. The reduction in the patent lives of m_0 and m_2 are shown as the shift from the light dotted lines to the dark dashed lines. In practice, the net present discounted profit for m_0 and m_2 under patent protection may be greater than V^f if time is treated as a discrete measure. The market entry of m_1 is delayed until the entry of m_2, while the entry of m_3 is delayed until m_2's shorter patent expires.

I focus my analysis on the market for antidepressants, in which Prozac was the first SSRI and was clearly a high-value innovation. I then assume that Zoloft provides significant therapeutic value beyond Prozac, while the three SSRI molecules that enter the market after Zoloft are "me-too"s.[6] While Paxil CR also entered the market during this time, it represents an advancement over Paxil in the formulation and not the molecule. For this reason, I combine Paxil and Paxil CR as one innovation in the policy experiments. Given that Zoloft was the first SSRI to follow Prozac, I extend

[6] Currently, there is no formal definition or explicit quality thresholds that distinguish high-value and "me-too" innovations.

Zoloft's patent breadth to the therapeutic class level and temporarily exclude these "me-too" innovations. However, Prozac's patent length is still limited so that its innovator earns the same net-present discounted profits under patent protection. This restriction only applies to later entrants in the SSRI class and therefore, innovations in other classes would not be directly affected.

Below, I present two counterfactuals and compare their results to those in Chapter 2. The first assumes that all "me-too" innovations that entered under the original policy also enter under the modified policy, once Prozac's shortened patent length expires. For the second counterfactual, I provide a framework which allows "me-too" innovators to anticipate the impact of the modified policy and re-optimize their entry decision before entering Phase III clinical trials. Innovators that choose to forgo additional drug development and eventual market entry would save the associated investment costs.

4.3.2 Exogenous Entry

Social Welfare under Exogenous Entry

The net discounted social welfare impact of the modified policy is the sum of the discounted effects on consumers (CV), insurers (Π^{ins}), and producers (Π^{diff}).[7] This is given by

$$SC = CV + \Pi^{ins} + \Pi^{diff}. \tag{4.1}$$

I assume that consumers and insurers have an annual discount rate of 5% while the producers' discount rate is 11%, which accounts for the innovator's risk of product failure during the product development process (DiMasi et al., 2003). The use of this higher producer discount rate means that, for a given amount of patent breadth, the innovator of the groundbreaking drug will require relatively less patent length in order to realize V^f. Under exogenous entry, consumers benefit from this shortened

[7] Producers include both innovators and manufacturers.

patent length due to the expedited entry of the generics on Prozac's molecule.[8] The implications for the "me-too" innovators is less clear. While they are able to enter the market sooner under the higher discount rate, they also place greater value on the time they are restricted from the market. However, I find that the final results are not qualitatively different when I use a 5% discount rate for producers.

As previously noted, prescription drug costs comprise only a small fraction of household income. Thus, I use compensating variation to calculate the impact that switching to the modified patent policy will have on consumers. Interestingly, this impact can be fully captured by the difference in log shares of the outside good under the two policies, magnified by the size of the market and translated into dollars by the disutility of price (copay) (Arcidiacono and Miller, 2011). For all consumers at time t, this is given by

$$CV_t = -\frac{M_t}{\alpha}\left[\ln\left(s_{0t}^{ante}\right) - \ln\left(s_{0t}^{post}\right)\right] \tag{4.2}$$

where s_{0t}^{ante} and s_{0t}^{post} denote the share of the outside good at time t under the current and modified policies, respectively. The total discounted welfare change is then

$$CV = \sum_{t=1}^{T} CV_t \cdot (1-d^c)^{t-1} \tag{4.3}$$

where d^c is the rate at which consumers discount utility.

While consumers pay only a fraction of the full drug prices, the rest of the price is paid by insurers. Therefore, insurer savings from the switch to the modified policy is given by

$$\Pi^{ins} = \sum_{t=1}^{T}\left\{\sum_{j=1}^{J}\left[(p_{jt}^{ante} - c_{jt}^{ante})s_{jt}^{ante} - (p_{jt}^{post} - c_{jt}^{post})s_{jt}^{post}\right]\cdot M_t \cdot (1-d^c)^{t-1}\right\}, \tag{4.4}$$

[8] In the case of endogenous entry, consumer welfare will depend on the choices made by the "me-too" innovators.

where the terms identified as *ante* and *post* correspond to the equilibrium prices and shares under the current and modified policies, respectively. Note that the insurers, like the consumers, are payers and so their expenditures are discounted by the consumer rate, d^c.

The profit of firm f at time t is

$$\Pi_{ft} = \sum_{m \in \mathcal{J}_{ft}} \sum_{j \in m} [(p_{jt} - mc_{jt}) M_t s_j(\boldsymbol{p}_t)] - a_{mt} - C_{ft} \tag{4.5}$$

where a_{mt} is the cost of advertising, C_{ft} is the fixed cost of production, and $s_j(\boldsymbol{p}_t)$ is the market share of product j and is a function of the prices of all products at time t. For the producers' net total welfare effect (innovators and generic manufacturers), the difference of each producer's profit under the current and modified policies is summed across all producers and discounted to time $t = 1$. That is,

$$\Pi^{diff} = \sum_{t=1}^{T} \left[\sum_{f=1}^{F} \left(\Pi_{ft}^{post} - \Pi_{ft}^{ante} \right) \cdot (1 - d^f)^{t-1} \right], \tag{4.6}$$

where d^f is the rate at which producers discount profits, and Π_{ft}^{ante} and Π_{ft}^{post} are producer f's profit under the current and modified policies, respectively.

For simplicity in implementing the simulations of the modified patent policies, I use the averages over time of both implied marginal cost, mc_j, and unobserved product heterogeneity, ξ_j, for each product j.

Results under Exogenous Entry

The first SSRI, Prozac, entered the antidepressant market in January 1988 and enjoyed an effective patent life of 13.5 years. Following Prozac, Zoloft emerged onto the market in February 1992 and its patent lasted 14.4years. During its patent-protected time on market, three other SSRI drugs entered the market: Paxil, Celexa,

and Lexapro.[9] I assume that these are "me-too" drugs, and restrict them from the market until Zoloft's patent expires under the modified policy. Under the original policy, I then calculate the present discounted profits generated by both Prozac and Zoloft while under patent protection. This amount is then set as the minimum profit requirement for each innovation under the modified policy. Given the restriction under the modified policy, I find that Zoloft's innovator is able to earn at least the same present discounted profits with a patent that expires in April 2002, reducing its patent life by 52 months (30%).[10] The delay of Paxil and Celexa also benefit the innovator of Prozac. To provide its innovator with approximately the same present discounted profits, Prozac's patent life is reduced by 26 months (21%).

Table 4.2 provides the impact of the policy switch on the "me-too"s. The effective patent life for Paxil and Celexa are shortened by 9.18 and 3.58 years, respectively. For Paxil, this is a reduction of nearly 90% of its patent protected time on market, while it is almost 60% for Celexa. On the other hand, Lexapro entered the market in August 2005 and so its effective patent life is unaffected. Once on the market, the "me-too" drugs compete against Prozac (fluoxetine), Zoloft (sertraline) and their generic variants. Discounted to January 1991, Paxil experienced a $930 million loss in profit (91% reduction) due to its delayed entry and competition against generic fluoxetine and sertraline. For Celexa, this loss was only $414 million, but this amounts to more than 96% of its profit under the original policy. The impact on Lexapro is exclusively from its competition with generic sertraline. The last row in Table 4.2 shows the impact of the generic versions of each of these "me-too" drugs. Under the orginal policy, generics on both Paxil (paroxetine) and Celexa (citalopram) enter before those on sertraline. The earlier entry by generics on sertraline results in a

[9] As previously stated, Paxil CR represents an advancement over Paxil in the formulation and not the molecule. For this reason, I combine Paxil and Paxil CR as one innovation in the policy experiments.

[10] Note that time in my data is in increments of months.

non-trivial impact on profits earned by generics on these subsequent molecules.

The total effect for each segment of the market is provided by Table 4.3. Under the counterfactual simulation, Prozac earned an additional $21 million and Zoloft earned an additional $6 million, primarily due to the discreteness of time in setting their new patent lengths. The impact of the policy switch generated more than $1.3 billion and $900 million in additional profits for producers of generic fluoxetine and sertraline, respectively. Note that I assume that the number and relative timing of entry among the generic fluoxetine and sertraline producers remains the same. The overall timing is simply advanced to the new patent expiration date for both molecules.[11] The total impact for "me-too" brands and generics are simply the totals of the figures in Table 4.2. As expected, the impact on the rest of the products in the market is fairly small. The net impact across all producers is a gain of nearly $700 million. Allowing additional generic entry on fluoxetine and sertraline would then reduce their super-normal profits and lead to a large and negative net impact across all producers. However, this potential negative impact on producers is overshadowed by the substantial savings by insurers, more than $8.2 billion (an 11.3% reduction in expenditures). This stems from the substantially lower cost to insurers when consumers purchase generics over brand name products and with the advanced timing of generic entry on both Prozac and Zoloft. Finally, consumers realize a small net gain due to this advanced timing of generic entry, despite the broadening of Zoloft's market exclusivity to temporarily restrict the entry of "me-too"s. The overall effect on social welfare is a $9.1 billion gain. While this net welfare result is smaller than the corresponding number reported in Chapter 2, the overall implications remain the same.

[11] For example, consider two generic firms, A and B, where Firm A enters two months before Firm B. Under the counterfactual, Firm A will still enter two months before Firm B, even though overall both enter the market earlier.

The above policy experiment examines the impact of allowing next-in-class products to be considered high-value innovations and receive the modified combination of patent breadth and length. However, it maintains the same entry decisions for subsequent entrants that are defined as "me-too"s. For the second policy experiment, I relax this assumption on the entry decisions by "me-too" innovators to provide a more robust approach to estimate the social welfare impact.

4.3.3 Endogenous Entry

Entry Re-optimization

I now consider the impact of allowing "me-too" innovators to anticipate the impact of the modified patent policy on their expected profits and re-optimize their decision to enter Phase III clinical trials.[12] I implement this by focusing on innovators that were observed to enter the market under the current policy and comparing their entry costs to their expected profits. Hence, an innovator will save its investment costs of Phase III if it chooses not to continue. For simplicity, I assume that entry of previously unseen products does not occur under the modified policy. Under the current policy, innovators enter in a sequential order $f^1, ..., f^n$ and then realize profits $\Pi^{1,ante}, ..., \Pi^{n,ante}$, respectively. It is also assumed that this order reflects the order in which innovators reach their decision point at the end of Phase II clinical trials. Finally, I assume a full information game where innovators see the product qualities, development costs, and time to market entry of all the other potential market entrants. Therefore, innovator f can anticipate the impact of the modified policy on the timing of when product j would be allowed to enter the market.

Let $\mathfrak{C}_{fj}$ be innovator f's fixed Phase III clinical trial costs for product j and assume $\mathfrak{C}_{fj} \sim \mathcal{F}_N(\mu, \sigma^2 | 0 \leqslant \kappa < \mathfrak{C}_{fj} < V_{fj}^{ante})$, where $\mathfrak{C}_{fj}$ is independent across

[12] By the end of Phase II clinical trials, innovators have usually gained their first significant evidence of efficacy and safety (DiMasi et al., 1991; Mossinghoff, 1999). I assume that this is sufficient to make an informed decision.

innovators and products, V_{fj}^{ante} is innovator f's net present discounted profit from product j under the current policy, κ is a lower bound on costs, and $\mathcal{F}_N$ is a truncated normal distribution:

$$\mathcal{F}_N = \frac{\Phi\left(\frac{\mathfrak{C}_{fj}-\mu}{\sigma}\right) - \Phi\left(\frac{\kappa-\mu}{\sigma}\right)}{\Phi\left(\frac{V_{fj}^{ante}-\mu}{\sigma}\right) - \Phi\left(\frac{\kappa-\mu}{\sigma}\right)}. \tag{4.7}$$

Innovator f will choose to send product j to Phase III clinical trials under the modified policy if $\mathfrak{C}_{fj} < V_{fj}^{post}$, where V_{fj}^{post} is innovator f's net present discounted profit from product j under the modified policy.[13]

In order to estimate the probability of each possible market outcome under the modified policy, I apply the following simple algorithm:

1. Draw $\mathfrak{C}_{fj}$ for each product.

2. Determine the re-optimized decision for each product using backward induction.

3. Repeat Steps 1 and 2 $\mathcal{N}$ times.

4. Finally, calculate λ_n, the probability of each possible market outcome, $n = 1, ..., N$.

When simulating the entry re-optimization, I use estimates (in December 2010 dollars) calculated by DiMasi et al. (2003) for average Phase III costs, μ = \$143 million, and standard deviations, σ = \$118 million, for approved drugs. DiMasi et al. (2003) also estimated that the average length of time from the start of Phase III to drug approval is 52 months. I use this estimate to calculate V_{fj} for innovator f and product j. Finally, I set κ to be \$1 million.

[13] Given that these products were approved by the FDA under the current policy, they would still be approved under the modified policy. The question is merely one of timing if products continue on to Phase III.

Social Welfare under Endogenous Entry

The social welfare calculation under endogenous entry is a simple analog of the exogenous case that includes probability weights for the N market outcomes. The equations corresponding to (4.2)-(4.6) for the counterfactual with endogenous entry for "me-too" are given by:

$$CV_{t,n} = -\frac{M_t}{\alpha}\left[\ln\left(s_{0t}^{ante}\right) - \ln\left(s_{0tn}^{post}\right)\right], \tag{4.8}$$

$$CV = \sum_{n=1}^{N} \lambda_n \left[\sum_{t=1}^{T} CV_{t,n} \cdot (1-d^c)^{t-1}\right], \tag{4.9}$$

$$\Pi^{ins} = \sum_{n=1}^{N} \lambda_n \left(\sum_{t=1}^{T}\left\{\sum_{j=1}^{J}\left[\left(p_{jt}^{ante} - c_{jt}^{ante}\right) s_{jt}^{ante} - \left(p_{jtn}^{post} - c_{jtn}^{post}\right) s_{jtn}^{post}\right] \cdot M_t \cdot (1-d^c)^{t-1}\right\}\right), \tag{4.10}$$

$$\text{and} \quad \Pi^{diff} = \sum_{n=1}^{N} \lambda_n \left\{\sum_{t=1}^{T}\left[\sum_{f=1}^{F}\left(\Pi_{ftn}^{post} - \Pi_{ft}^{ante}\right) \cdot (1-d^f)^{t-1}\right]\right\}. \tag{4.11}$$

Let $I_{jn}^{PhaseIII}$ be the expenditure saved when innovation j is abandoned rather than taken to Phase III clinical trials, discounted to time $t = 1$ using the rate d^f. The total expenditure saved across all such abandoned innovations is given by

$$I^{PhaseIII} = \sum_{n=1}^{N} \lambda_n \left(\sum_{j=1}^{J} I_{jn}^{PhaseIII}\right). \tag{4.12}$$

Finally, the discounted social welfare effect is then given by

$$SC = CV + \Pi^{ins} + \Pi^{diff} + I^{PhaseIII}. \tag{4.13}$$

Results under Endogenous Entry

As before, the "me-too" drugs may enter the market starting in April 2002. The lower and upper bound values that plugged into the truncated normal distribution

in equation (4.7) are provided in the first two rows of Table 4.4. To calculate the upper bound, the net present profit of each product is discounted back to the start of Phase III clinical trials. This is assumed to be 52 months prior to the orginal market entry date for all products. Note that all of the products have an upper bound that is substantially higher than the distribution mean of $143 million. The middle two rows of Table 4.4 give the average and standard deviation of draws from step (1) of the algorithm. Given that the "me-too" innovators make their decisions in sequential order, backward induction is used to determine the market outcome for each set of cost draws. The probability of entry for each drug is provided in the fifth row of the table. Lexapro will always go into Phase III clinical trials and eventually enter the market, while Paxil and Celexa will do so 18% and 6% of the time, respectively. The last row in the table provides the saved expenditure weighted by market outcome.

The impact of the policy switch on the "me-too"s is provided in Table 4.5. The first row of Table 4.2 matches the results in the first row here. Given the "me-too"s ability to reoptimize their entry decision, it is intuitive to expected that profit loss for the "me-too" brands would be lower. Summing the saved expenditure and the change in product profit easily confirms this expectation. The impact on the "me-too" generics is more closely tied to the entry decisions by the corresponding innovators. Generic entry on that molecule is assumed to never occur if a brand product is abandoned by its innovator. Lexapro is shown to benefit considerably from the low entry probability of both Paxil and Celexa. My data does not capture generic entry on Lexapro's molecule.

The net welfare effect for each segment of the market is presented in Table 4.6. The impact on generic versions of Prozac and Zoloft is now larger due to the limited competition when the other "me-too" products are abandoned. The seventh row of the table shows that the other products on the market also enjoy this benefit, though to a much smaller degree. Overall, the producers gain a profit of nearly $840 million.

By abandoning their products prior to Phase III, these innovators also saved $288 million in corresponding expenditures. The welfare of both insurers and consumers decreases, mostly due to the near certain loss of both paroxetine and citalopram. However, the overall effect is a social welfare gain of $9.3 billion, which is larger than the modified policy with exogenous entry.

4.4 Conclusion

This chapter extends the analysis in Chapter 2 to allow for a more generalized framework. In that chapter, the first pharmaceutical product innovation that enters a therapeutic class is assumed to be high-value while those innovations that follow are assumed to provide relatively little, if any, added therapeutic value beyond the first. Using the same data and demand model estimates, I consider the potential welfare effects of allowing these later to be considered high-value products and providing them with greater patent breadth and shorter patent length. In this chapter, I show that the results presented in Chapter 2 are robust to adjustment in the modified policy framework.

However, how innovations are determined to be either high quality or "me-too" innovations and the way in which they are treated once this determination is made are important issues. Currently, there is no definition or explicit quality thresholds to distinguish between high-value and "me-too" innovations. It is therefore necessary to rely on *ad hoc* assumptions to specify these thresholds. If high value innovations are not identified as such, there is a potential for significant welfare loss, which may also have a negative impact on the long-run innovation flow. On the other hand, if the assumption sufficiently covers all innovations that are truly high value, there is relatively little concern about the potential of misidentifying a "me-too" as a high value product. The reason for this stems from that fact that if all products are assumed to be high value, this modified patent is never applied and we are simply

left with our current policy.

The results in this chapter further support the potential for meaningful social gains from exploring modified patent policies. However, my analysis still relies on a variety of assumptions that simplify the problem, but also limit the generalizability of my conclusions. For example, I still abstract away from any uncertainty consumers may have of the quality of new products introductions. If consumers learn about this quality from each other, then the higher counterfactual price on Prozac would induce more price-sensitive consumers to switch to generic versions. In turn, this would speed up consumers' learning process as well as the adoption rate of these generics. Therefore, the modified patent policy could potentially further increase the competitive pressure on Prozac's innovator after patent expiration. It is left for future work to examine the effects of relaxing this and other assumptions, including those restricting the dynamic behavior of insurers and other market participants.

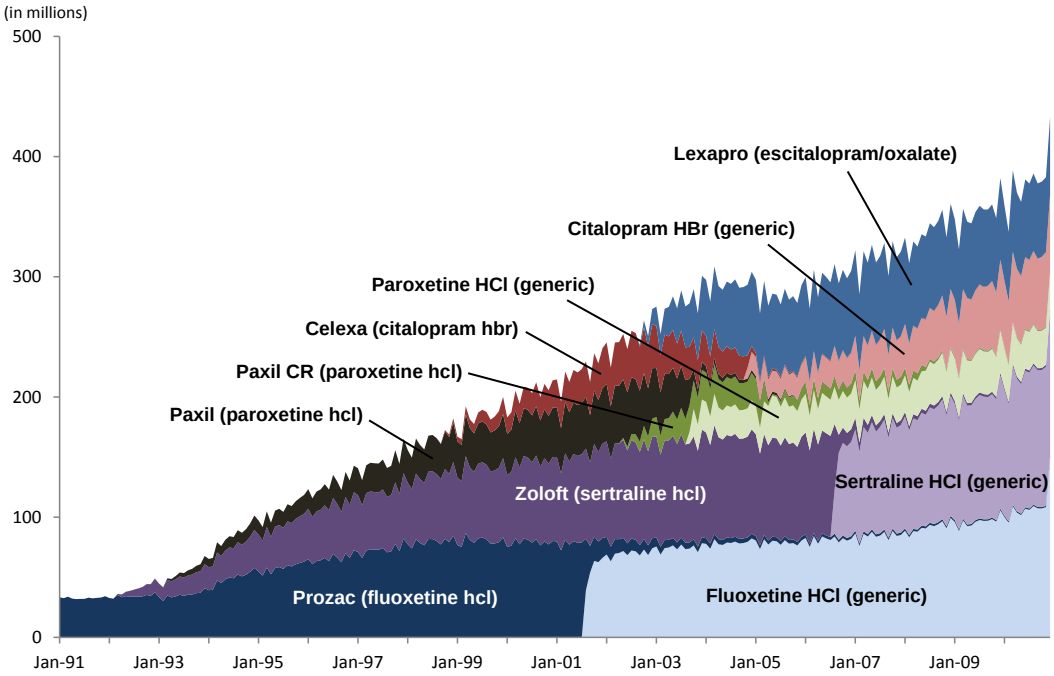


FIGURE 4.1: Area Plot of Monthly Quatity Sales for the Top SSRI Molecules with Standardized Daily Doses: January 1991 – December 2010

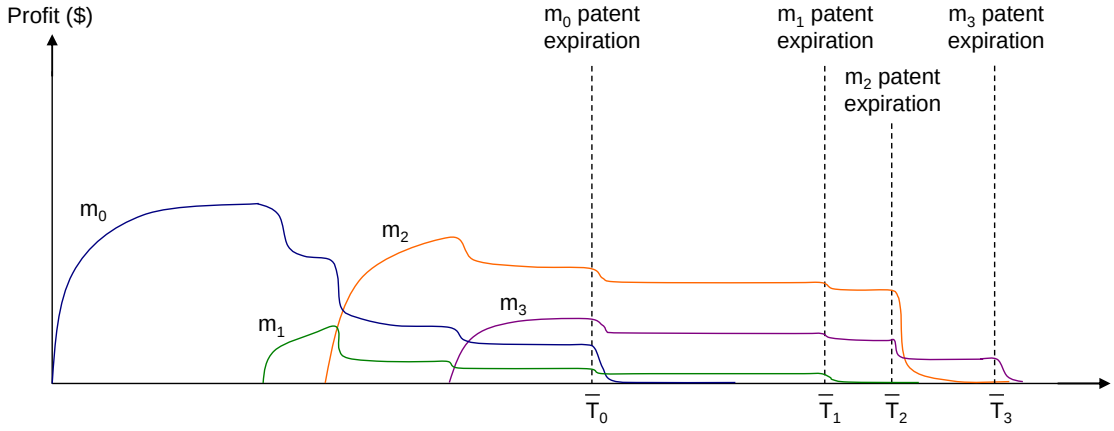


FIGURE 4.2: Demonstrative for Current Patent Policy

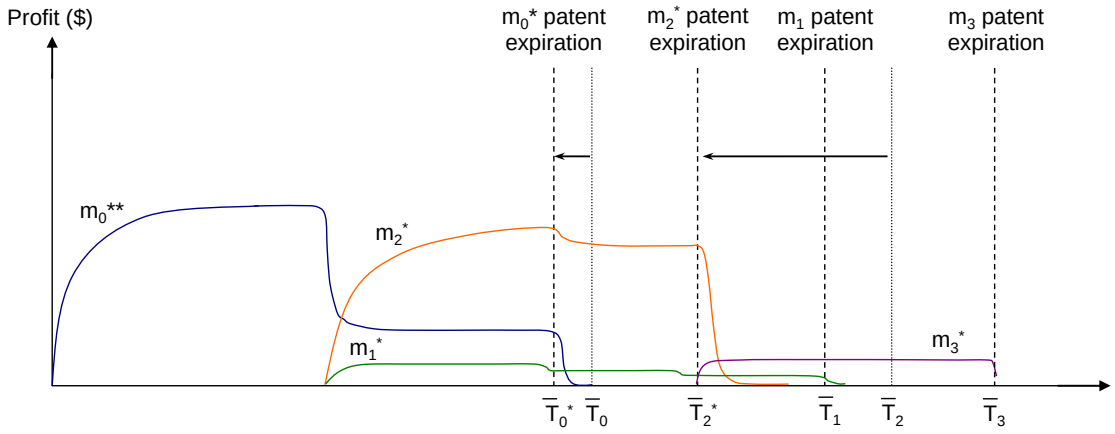


FIGURE 4.3: Demonstrative for Modified Patent Policy

Table 4.1: Drug Details

Drug Class	Molecule[a]	1^{st} Brandname	1^{st} Launch	1^{st} Patent Exp.[b]	Number of Generics[c]
NGA	bupropion	Wellbutrin	1986m3	1999m12	8
NGA	venlafaxine	Effexor	1994m2	2006m8	14
NGA	nefazodone	Serzone	1995m1	2003m9	7
NGA	mirtazapine	Remeron	1996m7	2003m1	11
NGA	duloxetine	Cymbalta	2004m8	–	–
SSRI	fluoxetine	Prozac	1988m1	2001m7	18
SSRI	sertraline	Zoloft	1992m2	2006m6	17
SSRI	paroxetine	Paxil	1993m1	2003m5	9
SSRI	citalopram	Celexa	1998m8	2004m10	17
SSRI	escitalopram/oxalate	Lexapro	2002m8	–	–

Source: SDI Database.
[a] Selected sample of the top selling antidepressants.
[b] First patent expiration values are missing if the patents are still active on December 2010.
[c] Generics refers to the number of generic producers that compete under a given molecule.

Table 4.2: Impact of Modified Policy on "Me-Too" Drugs with Exogenous Entry

	Change in Levels			Percentage Change		
Change in:	Paxil	Celexa	Lexapro	Paxil	Celexa	Lexapro
effective patent life[a]	-9.17	3.58	0	88.0%	58.1%	0.0%
PV(brand profit)[b]	-930	-414	-98	-91.2%	-96.0%	-6.8%
PV(generic profit)[b]	-39	-14	0	-8.4%	-5.3%	0%

[a] Effective patent life is in years.
[b] All dollars are in millions and discounted to January 1991 with a rate of 11%.

Table 4.3: Present Value Welfare Under Exogenous Entry

Change In	Dollars[a]	% Change
Prozac profit[b]	21	0.8%
generic Prozac profit[b]	1304	88.8%
Zoloft profit[b]	6	0.1%
generic Zoloft profit[b]	952	206.2%
'me-too' brand profit[b]	-1442	-49.8%
'me-too' generic profit[b]	-53	-7.3%
other non-SSRI profit[b]	-99	-1.1%
all firms' profit[b]	689	3.1%
insurer savings[c]	8291	-11.3%
consumer welfare[c]	166	0.8%
social welfare	9146	7.9%

[a] Dollars are in millions and discounted to January 1991.
[b] Firms' profits are discounted at 11%.
[c] Insurer savings and consumer welfare are discounted at 5%.

Table 4.4: Distribution Bounds and Average Costs of Phase III Clinical Trials[a]

	Paxil	Celexa	Lexapro
lower bound[b]	1	1	1
upper bound[b]	776	630	3363
mean(cost)[c]	169	171	168
sd(cost)[c]	98	99	98
Prob(entry)[c]	18.1%	5.8%	100%
$I^{PhaseIII}$	178	110	–

[a] All dollar values are in millions.
[b] Lower and upper bounds of the products' respective truncated normal distributions. The upper bounds are calculated as the net present value profit of each product, discounted to the start of Phase III clinical trials, 52 months prior to market entry.
[c] Based on 10,000 random draws for each product.

Table 4.5: Impact of Modified Policy by Molecule[a]

	Change in Levels			Percentage Change		
Change in:	Paxil	Celexa	Lexapro	Paxil	Celexa	Lexapro
effective patent life[a]	-9.17	3.58	0	88.0%	58.1%	0.0%
PV(brand profit)[c]	-1002	-430	184	-98.3%	-99.7%	12.7%
PV(generic profit)[c]	-379	-247	0	-81.9%	-93.9%	0%

[a] Effective patent life is in years.
[b] Phase III clinical trial costs are weighted by entry decisions and then discounted or inflated to January 1991.
[c] Profits are calculated according to equation (4.11), then weighted by entry decisions and discounted to January 1991. All dollars are in millions.

Table 4.6: Present Value Welfare Under Endogenous Entry

Change In	Dollars[a]	% Change
Prozac profit[b]	21	0.8%
generic Prozac profit[b]	1467	99.9%
Zoloft profit[b]	6	0.1%
generic Zoloft profit[b]	1167	252.8%
'me-too' brand profit[b]	-1248	-43.1%
'me-too' generic profit[b]	-627	-86.2%
other non-SSRI profit[b]	53	0.6%
all firms' profit[b]	840	3.8%
saved expenditure[b]	288	
insurer savings[c]	8258	-11.3%
consumer welfare[c]	-84	0.4%
social welfare	9301	8.1%

[a] Dollars are in millions and discounted to January 1991.
[b] Firms' profits are discounted at 11%.
[c] Insurer savings and consumer welfare are discounted at 5%.

Appendix A

Appendix for Chapter 2

A.1 Demand Equation

Suppose consumers choose from an assortment of products which belong to two levels of groupings. Let g index the upper level and m_g index the lower, subgroup level. The indirect utility that consumer i gets from product j at time t is given by

$$u_{ijt} = \delta_{jt} + \psi_{ijt}$$

$$\text{where} \quad \delta_{jt} = x_{jt}\beta_j + \alpha p_{jt}^{\phi} + \gamma ln(a_{m_g t}) + \xi_{jt}$$

$$\text{and} \quad \psi_{ijt} = \zeta_{igt} + (1-\sigma_g)\zeta_{im_g t} + (1-\sigma_g)(1-\sigma_{m_g})\varepsilon_{ijt}.$$

I now define $\eta = [1-(1-\sigma_g)(1-\sigma_{m_g})] \in [0,1)$ and so,

$$\sigma_{m_g} = 1 - \frac{1-\eta}{1-\sigma_g}. \tag{A.1}$$

The market share of product j as a fraction of the total lower-nesting group is equivalent to the probability of a consumer purchasing a product from among those in the subgroup m_g:

$$s_{j/m_g} = \frac{e^{\delta_j/(1-\eta)}}{D_m} \quad \text{where} \quad D_m = \sum_{k \in J_{m_g}} e^{\delta_k/(1-\eta)}. \tag{A.2}$$

Similarly, the market share of subgrouping m_g as a fraction of the total upper-nesting group is equivalent to the probability that a consumer purchases from among the product within subgrouping m_g from among those in group g

$$s_{m_g} = \frac{D_m^{(1-\sigma_{m_g})}}{D_g} \quad \text{where} \quad D_g = \sum_{k \in J_g} D_m^{(1-\sigma_{m_g})}. \tag{A.3}$$

Next, the probability that a consumer chooses a product from grouping g from among all products is given by

$$s_g = \frac{D_g^{(1-\sigma_g)}}{D} \quad \text{where} \quad D = \sum_{k \in J} D_g^{(1-\sigma_g)}. \tag{A.4}$$

Finally, the probability of the consumer choosing the outside option and not purchasing any of the products in the market is given by

$$s_0 = \frac{1}{D}. \tag{A.5}$$

The overall market share for product j is

$$\begin{aligned} s_j &= s_{j/m_g} \cdot s_{m_g} \cdot s_g \\ &= e^{\delta_j/(1-\eta)} D_m^{-\sigma_{m_g}} D_g^{-\sigma_g} D^{-1}. \end{aligned} \tag{A.6}$$

Taking natural logs of this equation and substituting in the natural log of (5) gives

$$ln(s_j) = \frac{\delta_j}{1-\eta} - \sigma_{m_g} ln(D_m) - \sigma_g ln(D_g) + ln(s_0). \tag{A.7}$$

Rearranging this equation and combining it with the natural logs of (2) and (3) allows for the following steps:

$$\begin{aligned} ln(s_j) - ln(s_0) &= \frac{\delta_j}{1-\eta} - \sigma_g \left[(1-\sigma_{m_g})ln(D_m) - ln(s_{m_g})\right] - \sigma_{m_g} ln(D_m) \\ &= \frac{\delta_j}{1-\eta} + \sigma_g ln(s_{m_g}) - \left[\sigma_{m_g} + \sigma_g(1-\sigma_{m_g})\right] ln(D_m) \\ &= \frac{\delta_j}{1-\eta} + \sigma_g ln(s_{m_g}) - \eta ln(D_m) \\ &= \frac{\delta_j}{1-\eta} + \sigma_g ln(s_{m_g}) - \eta \left[\frac{\delta_j}{1-\eta} - ln(s_{j/m_g})\right] \\ &= \delta_j + \sigma_g ln(s_{m_g}) + \eta ln(s_{j/m_g}). \end{aligned} \tag{A.8}$$

A.2 Elasticities

The price elasticity, $\eta^{elast}_{s_j,c_k}$, is the sensitivity of product j's market share to changes in product k's copay:

$$\eta^{elast}_{s_j,c_k} = \frac{\partial s_j}{\partial c_k} \cdot \frac{c_k}{s_j} \tag{A.9}$$

$$\text{where} \quad s_j = s_{j/m_g} \cdot s_{m_g} \cdot s_g = e^{\delta_j/(1-\eta)} D_m^{-\sigma_{m_g}} D_g^{-\sigma_g} D^{-1}.$$

For $j = k$,

$$\begin{aligned} \frac{\partial s_j}{\partial c_j} &= \frac{\alpha}{1-\eta} D_m^{-\sigma_{m_g}} D_g^{-\sigma_g} D^{-1} e^{\delta_j/(1-\eta)} \\ &\quad - \sigma_{m_g} \frac{\alpha}{1-\eta} e^{2\delta_j/(1-\eta)} D_m^{-\sigma_{m_g}-1} D_g^{-\sigma_g} D^{-1} \\ &\quad - \sigma_g(1-\sigma_{m_g}) \frac{\alpha}{1-\eta} e^{2\delta_j/(1-\eta)} D_m^{-2\sigma_{m_g}} D_g^{-\sigma_g-1} D^{-1} \\ &\quad - (1-\sigma_g)(1-\sigma_{m_g}) \frac{\alpha}{1-\eta} e^{2\delta_j/(1-\eta)} D_m^{-2\sigma_{m_g}} D_g^{-2\sigma_g} D^{-2} \\ &= \frac{\alpha}{1-\eta} \left[s_j - \sigma_{m_g} s_{j/m_g} s_j - \sigma_g(1-\sigma_{m_g}) s_{j/m_g} s_{m_g} s_j - (1-\eta) s_j s_j\right] \\ &= \frac{\alpha}{1-\eta} s_j \left[1 - \sigma_{m_g} s_{j/m_g} - \sigma_g(1-\sigma_{m_g}) s_{j/m_g} s_{m_g} - (1-\eta) s_j\right]. \end{aligned} \tag{A.10}$$

For $j \neq k$, but $m_j = m_k$,

$$\begin{aligned}
\frac{\partial s_j}{\partial c_k} &= -\sigma_{m_g}\frac{\alpha}{1-\eta}e^{\delta_k/(1-\eta)}e^{\delta_j/(1-\eta)}D_m^{-\sigma_{m_g}-1}D_g^{-\sigma_g}D^{-1} \\
&\quad - \sigma_g(1-\sigma_{m_g})\frac{\alpha}{1-\eta}e^{\delta_k/(1-\eta)}e^{\delta_j/(1-\eta)}D_m^{-2\sigma_{m_g}}D_g^{-\sigma_g-1}D^{-1} \\
&\quad - (1-\sigma_g)(1-\sigma_{m_g})\frac{\alpha}{1-\eta}e^{\delta_k/(1-\eta)}e^{\delta_j/(1-\eta)}D_m^{-2\sigma_{m_g}}D_g^{-2\sigma_g}D^{-2} \\
&= -\frac{\alpha}{1-\eta}\left[\sigma_{m_g}s_{k/m_g}s_j + \sigma_g(1-\sigma_{m_g})s_{k/m_g}s_{m_g}s_j + (1-\eta)s_k s_j\right] \\
&= -\frac{\alpha}{1-\eta}s_j\left[\sigma_{m_g}s_{k/m_g} + \sigma_g(1-\sigma_{m_g})s_{k/m_g}s_{m_g} + (1-\eta)s_k\right] \qquad \text{(A.11)}
\end{aligned}$$

For $m_j \neq m_k$, but $g_j = g_k$,

$$\frac{\partial s_j}{\partial c_k} = -\frac{\alpha}{1-\eta}s_j\left[\sigma_g(1-\sigma_{m_g})s_{k/m_g}s_{m_g} + (1-\eta)s_k\right] \qquad \text{(A.12)}$$

For $g_j \neq g_k$,

$$\frac{\partial s_j}{\partial c_k} = -\alpha s_k s_j \qquad \text{(A.13)}$$

The own-price elasticity is then

$$\eta_{own} = \frac{\alpha}{1-\eta}c_{jt}\left[1 - \sigma_{m_g}s_{jt/m_g} - \sigma_g(1-\sigma_{m_g})s_{jt/m_g}s_{m_g t} - (1-\eta)s_{jt}\right]. \qquad \text{(A.14)}$$

For the analysis in this paper, the most meaninful cross-price elasticities are those within a therapeutic class, but across molecules (lower level nests) and those across therapeutic classes (upper level nests):

$$\eta_{x\text{-}molec.} = -\frac{\alpha}{1-\eta}c_{jt}\left[\sigma_g(1-\sigma_{m_g})s_{kt/m_g}s_{m_g t} + (1-\eta)s_{kt}\right] \quad \text{and} \qquad \text{(A.15)}$$

$$\eta_{x\text{-}class} = -\alpha c_{jt}s_{jt}, \qquad \text{(A.16)}$$

respectively.

Appendix B

Appendix for Chapter 3

B.1 Derivation of Micro Moments

We begin by denoting the probability of contracting the disease treated by H2s or PPIs by ϕ and the probability of becoming well by ψ. These probabilities are assumed to be independent of consumer demographics and unobserved types. If w^* denotes the probability of being well, then $w^* = \frac{\psi}{\psi+\phi}$.[1] Suppose there are two types of consumers and τ denotes the proportion of those who are type 2. Let p_{1t} and p_{2t} denote the probabilities of buying a product on the market at time t for consumers of type 1 and type 2, respectively.

Starting with the set of moments of buying versus not buying any products on the market, the probability purchasing at $t+1$ conditional on purchasing at t is then:

$$\begin{aligned} Pr(d_{t+1}=1|d_t=1) &= \frac{Pr(d_t=1,d_{t+1}=1)}{Pr(d_t=1)} \\ &= \frac{(1-w^*)(1-\psi)((1-\tau)p_{1t}p_{1t+1}+\tau p_{2t}p_{2t+1})}{(1-w^*)((1-\tau)p_{1t}+\tau p_{2t})} \\ &= \frac{(1-\psi)((1-\tau)p_{1t}p_{1t+1}+\tau p_{2t}p_{2t+1})}{((1-\tau)p_{1t}+\tau p_{2t})}. \end{aligned}$$

If we then denote a consumer's health by h_t (1 is healthy and 0 is sick) and the

[1] Notice that $1-w^*$ is the prevalence of the disease.

probability purchasing at $t+2$ conditional on purchasing at t is:

$$\begin{aligned}
Pr(d_{t+2}=1|d_t=1) &= \frac{Pr(d_t=1,d_{t+2}=1|h_{t+1}=0)+Pr(d_t=1,d_{t+2}=1|h_{t+1}=1)}{Pr(d_t=1)} \\
&= \frac{Pr(d_t=1,d_{t+1}=1,d_{t+2}=1)+Pr(d_t=1,d_{t+1}=0,d_{t+2}=1)}{Pr(d_t=1)} \\
&\quad + \frac{Pr(d_t=1,d_{t+2}=1|h_{t+1}=1)}{Pr(d_t=1)} \\
&= \frac{(1-w^*)(1-\psi)^2[(1-\tau)p_{1t}p_{1t+1}p_{1t+2}+\tau p_{2t}p_{2t+1}p_{2t+2}]}{Pr(d_t=1)} \\
&\quad + \frac{(1-w^*)(1-\psi)^2[(1-\tau)p_{1t}(1-p_{1t+1})p_{1t+2}+\tau p_{2t}(1-p_{2t+1})p_{2t+2}]}{Pr(d_t=1)} \\
&\quad + \frac{(1-w^*)\psi\phi[(1-\tau)p_{1t}p_{1t+2}+\tau p_{2t}p_{2t+2}]}{Pr(d_t=1)} \\
&= \frac{(1-w^*)[(1-\psi)^2+\psi\phi][(1-\tau)p_{1t}p_{1t+2}+\tau p_{2t}p_{2t+2}]}{(1-w^*)((1-\tau)p_{1t}+\tau p_{2t})}.
\end{aligned}$$

If we accept that $p_{1t+2} \approx p_{1t+1}$ and $p_{2t+2} \approx p_{2t+1}$, then

$$\begin{aligned}
Pr(d_{t+2}=1|d_t=1) &\approx \frac{(1-w^*)[(1-\psi)^2+\psi\phi][(1-\tau)p_{1t}p_{1t+1}+\tau p_{2t}p_{2t+1}]}{Pr(d_t=1)} \\
&\approx \frac{[(1-\psi)^2+\psi\phi](1-w^*)(1-\psi)[(1-\tau)p_{1t}p_{1t+1}+\tau p_{2t}p_{2t+1}]}{(1-\psi)Pr(d_t=1)} \\
&\approx \frac{[(1-\psi)^2+\psi\phi]}{(1-\psi)}Pr(d_{t+1}=1|d_t=1) \quad \text{where} \quad \phi=\psi\frac{1-w^*}{w^*} \qquad \text{(B.1)}
\end{aligned}$$

This equation then allows us to calculate the unknowns, ψ and ϕ.

The probability of purchasing at $t+1$ and $t+2$ conditional on purchasing at t is:

$$\begin{aligned}
Pr(d_{t+1}=1,d_{t+2}=1|d_t=1) &= \frac{Pr(d_t=1,d_{t+1}=1,d_{t+2}=1)}{Pr(d_t=1)} \\
&= \frac{(1-w^*)(1-\psi)^2[(1-\tau)p_{1t}p_{1t+1}p_{1t+2}+\tau p_{2t}p_{2t+1}p_{2t+2}]}{(1-w^*)((1-\tau)p_{1t}+\tau p_{2t})} \\
&= \frac{(1-\psi)^2[(1-\tau)p_{1t}p_{1t+1}p_{1t+2}+\tau p_{2t}p_{2t+1}p_{2t+2}]}{((1-\tau)p_{1t}+\tau p_{2t})}.
\end{aligned}$$

Now, we move on to the set of moments specific to the product characteristics denoted by k. Let p_{1t}^k and p_{2t}^k denote the probabilities of buying a product with characteristic k on the market at time t for consumers of type 1 and type 2, respectively. The probability of purchasing a product with characteristic k at $t+1$ conditional on purchasing a product with characteristic k at t is:

$$\begin{aligned} Pr(d_{t+1}^k = 1 | d_t^k = 1) &= \frac{Pr(d_t^k = 1, d_{t+1}^k = 1)}{Pr(d_t^k = 1)} \\ &= \frac{(1-w^*)(1-\psi)((1-\tau)p_{1t}^k p_{1t+1}^k + \tau p_{2t}^k p_{2t+1}^k)}{(1-w^*)((1-\tau)p_{1t}^k + \tau p_{2t}^k)} \\ &= \frac{(1-\psi)((1-\tau)p_{1t}^k p_{1t+1}^k + \tau p_{2t}^k p_{2t+1}^k)}{(1-\tau)p_{1t}^k + \tau p_{2t}^k}. \end{aligned}$$

The probability of purchasing any product at time t and a product with characteristic k at $t+2$ conditional on purchasing a product with characteristic k at t is:

$$\begin{aligned} Pr(d_{t+1} = 1, d_{t+2}^k = 1 | d_t^k = 1) &= \frac{Pr(d_t^k = 1, d_{t+1} = 1, d_{t+2}^k = 1)}{Pr(d_t^k = 1)} \\ &= \frac{(1-w^*)(1-\psi)^2((1-\tau)p_{1t}^k p_{1t+1} p_{1t+2}^k + \tau p_{2t}^k p_{2t+1} p_{2t+2}^k)}{(1-w^*)((1-\tau)p_{1t}^k + \tau p_{2t}^k)} \\ &= \frac{(1-\psi)^2((1-\tau)p_{1t}^k p_{1t+1} p_{1t+2}^k + \tau p_{2t}^k p_{2t+1} p_{2t+2}^k)}{(1-\tau)p_{1t}^k + \tau p_{2t}^k}. \end{aligned}$$

Finally, the probability of purchasing a product with characteristic k at time t and $t+2$ conditional on purchasing a product with characteristic k at t is:

$$\begin{aligned} Pr(d_{t+1}^k = 1, d_{t+2}^k = 1 | d_t^k = 1) &= \frac{Pr(d_t^k = 1, d_{t+1}^k = 1, d_{t+2}^k = 1)}{Pr(d_t^k = 1)} \\ &= \frac{(1-w^*)(1-\psi)^2((1-\tau)p_{1t}^k p_{1t+1}^k p_{1t+2}^k + \tau p_{2t}^k p_{2t+1}^k p_{2t+2}^k)}{(1-w^*)((1-\tau)p_{1t}^k + \tau p_{2t}^k)} \\ &= \frac{(1-\psi)^2((1-\tau)p_{1t}^k p_{1t+1}^k p_{1t+2}^k + \tau p_{2t}^k p_{2t+1}^k p_{2t+2}^k)}{(1-\tau)p_{1t}^k + \tau p_{2t}^k}. \end{aligned}$$

The micro moments calculated from the MarketScan data are presented in Table B.1. Using the equation B.1 and the first set of moments in Table B.1, we are able to calculate

ϕ and ψ, as presented in Table B.2. Noting that the values for the period 1996 to 2004 greatly differ from those in the period 2005 to 2009, we believe this implies consumers are recovering faster from uclers and other related health problems. Assuming the same probability of contracting the disease treated by H2s and PPIs, ϕ_2, we can then calculate a new probability of becoming well, ψ_2, as well as a new prevalence rate of having the disease, $prev_2$.

Table B.1: Moments from MarketScan

Dimension	Moments	Avg.	1996–2004	2005-2009
Buy vs Not Buy	$Pr(d_{t+1} = 1 \mid d_t = 1)$	0.7495	0.7401	0.7665
	$Pr(d_{t+2} = 1 \mid d_t = 1)$	0.7003	0.7033	0.6948
	$Pr(d_{t+1} = 1, d_{t+2} = 1 \mid d_t = 1)$	0.611	0.6063	0.6195
H2 vs PPI	$Pr(d^H_{t+1} = 1 \mid d^H_t = 1)$	0.6482	0.6530	0.6398
	$Pr(d_{t+1} = 1, d^H_{t+2} = 1 \mid d^H_t = 1)$	0.4929	0.5057	0.4700
	$Pr(d^H_{t+1} = 1, d^H_{t+2} = 1 \mid d^H_t = 1)$	0.4859	0.5003	0.4599
	$Pr(d^P_{t+1} = 1 \mid d^P_t = 1)$	0.7599	0.7525	0.7731
	$Pr(d_{t+1} = 1, d^P_{t+2} = 1 \mid d^P_t = 1)$	0.6244	0.6219	0.6291
	$Pr(d^P_{t+1} = 1, d^P_{t+2} = 1 \mid d^P_t = 1)$	0.6213	0.6180	0.6274
Brand vs Generic	$Pr(d^B_{t+1} = 1 \mid d^B_t = 1)$	0.7485	0.7421	0.7601
	$Pr(d_{t+1} = 1, d^B_{t+2} = 1 \mid d^B_t = 1)$	0.6085	0.6069	0.6115
	$Pr(d^B_{t+1} = 1, d^B_{t+2} = 1 \mid d^B_t = 1)$	0.6065	0.6049	0.6093
	$Pr(d^G_{t+1} = 1 \mid d^G_t = 1)$	0.6778	0.6417	0.743
	$Pr(d_{t+1} = 1, d^G_{t+2} = 1 \mid d^G_t = 1)$	0.5272	0.4917	0.591
	$Pr(d^G_{t+1} = 1, d^G_{t+2} = 1 \mid d^G_t = 1)$	0.5229	0.4866	0.5881
Capsule vs Tablet	$Pr(d^C_{t+1} = 1 \mid d^C_t = 1)$	0.5052	0.5409	0.441
	$Pr(d_{t+1} = 1, d^C_{t+2} = 1 \mid d^C_t = 1)$	0.4662	0.4922	0.4194
	$Pr(d^C_{t+1} = 1, d^C_{t+2} = 1 \mid d^C_t = 1)$	0.3664	0.3959	0.3134
	$Pr(d^T_{t+1} = 1 \mid d^T_t = 1)$	0.4661	0.4765	0.4474
	$Pr(d_{t+1} = 1, d^T_{t+2} = 1 \mid d^T_t = 1)$	0.4158	0.4242	0.4007
	$Pr(d^T_{t+1} = 1, d^T_{t+2} = 1 \mid d^T_t = 1)$	0.3229	0.3318	0.307

Table B.2: Probabilites of Ulcers

	Avg.	1996–2004	2005-2009
ψ	0.0668	0.0506	0.0961
ϕ	0.0167	0.0126	0.0240
ϕ_2	0.0126	0.0126	0.0126
ψ_2	0.0664	0.0506	0.0949
$prev_2$	0.1708	0.2000	0.1183

B.2 Elasticities

Let $s_j^{[ins]}$ and $s_j^{[unins]}$ denote the respective shares of product j among consumers who are insured and uninsured. The share that firm f sees for its product j is then given by:

$$\begin{aligned} s_j &= \rho s_j^{[ins]} + (1-\rho) s_j^{[unins]} \\ &= \rho \frac{\exp(\alpha b p_j^a + X\beta)}{\sum_l \exp(\delta_l^{[ins]})} + (1-\rho) \frac{\exp(\alpha p_j + X\beta)}{\sum_l \exp(\delta_l^{[unins]})} \end{aligned}$$

where the copay equation is given by $c_j = bp_j^a$.

The partial derivative of s_j with respect to p_j is then given by:

$$\begin{aligned} \frac{\partial s_j}{\partial p_j} &= \rho\alpha b a p_j^{a-1} \frac{\exp(\alpha b p_j^a + X\beta)}{\sum_l \exp(\delta_l^{[ins]})} - \rho\alpha b a p_j^{a-1} \exp(\alpha b p_j^a + X\beta) \frac{\exp(\alpha b p_j^a + X\beta)}{(\sum_l \exp(\delta_l^{[ins]}))^2} \\ &\quad + (1-\rho)\alpha \frac{\exp(\alpha p_j + X\beta)}{\sum_l \exp(\delta_l^{[unins]})} - (1-\rho)\alpha \exp(\alpha p_j + X\beta) \frac{\exp(\alpha p_j + X\beta)}{(\sum_l \exp(\delta_l^{[unins]}))^2} \\ &= \rho\alpha b a p_j^{a-1} s_j^{[ins]} - \rho\alpha b a p_j^{a-1} s_j^{[ins]} s_j^{[ins]} + (1-\rho)\alpha s_j^{unins} - (1-\rho)\alpha s_j^{unins} s_j^{unins} \\ &= \rho\alpha b a p_j^{a-1} s_j^{[ins]} (1 - s_j^{[ins]}) + (1-\rho)\alpha s_j^{[unins]} (1 - s_j^{[unins]}) \end{aligned}$$

The partial derivative of s_j with respect to p_k is then given by:

$$\begin{aligned} \frac{\partial s_j}{\partial p_k} &= -\rho\alpha b a p_k^{a-1} \exp(\alpha b p_k^a + X\beta) \frac{\exp(\alpha b p_j^a + X\beta)}{(\sum_l \exp(\delta_l^{[ins]}))^2} \\ &\quad -(1-\rho)\alpha \exp(\alpha p_k + X\beta) \frac{\exp(\alpha p_j + X\beta)}{(\sum_l \exp(\delta_l^{[unins]}))^2} \\ &= -\rho\alpha b a p_k^{a-1} s_k^{[ins]} s_j^{[ins]} - (1-\rho)\alpha s_k^{[unins]} s_j^{[unins]} \end{aligned}$$

If we then follow the elasticity equations, we get:

$$\begin{aligned}
\eta_{own} &= \frac{\partial s_j}{\partial p_j}\frac{p_j}{s_j} \\
&= \left[\rho\alpha bap_j^{a-1}s_j^{[ins]}(1-s_j^{[ins]}) + (1-\rho)\alpha s_j^{[unins]}(1-s_j^{[unins]})\right]\frac{p_j}{s_j} \\
\eta_{cross} &= \frac{\partial s_j}{\partial p_k}\frac{p_k}{s_j} \\
&= \left[-\rho\alpha bap_k^{a-1}s_k^{[ins]}s_j^{[ins]} - (1-\rho)\alpha s_k^{[unins]}s_j^{[unins]}\right]\frac{p_k}{s_j}
\end{aligned}$$

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Biography

Yair Taylor was born in Tiberias, Israel on December 8, 1980. He earned his B.A. in Applied Mathematics and Economics from the University of California, Berkeley in 2003. Finding a particular interest in the interaction of firms in the market, Yair then went on to work in economic litigation consulting for Cornerstone Research, where he focused on cases involving antitrust, intellectual property, and product liability.

In 2008, Yair returned to academia and earned his Masters in Economics from Duke University in 2009 and his PhD in Economics from Duke University in 2014. As a graduate student, he specialized in Industrial Organization. In April 2014, he won the "Best Rising Star Paper Prize" at the 12th Annual International Industial Organization Conference. After graduation, Yair will join the Economic Analysis Group (EAG) of the Antitrust Division at the Department of Justice, located in Washington, D.C. The EAG's mission is to promote free and fair competition as well as maintain the integrity of our markets across virtually all industries.